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OVARIAN NEOPLASMS

A Collective Review of the Recent Literature

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THE range of variety exhibited by neoplasms in the ovary is not duplicated in any other organ of the body, and this range is being continually expanded by the addition, from time to time, of what appear to be new oncologic entities. The discovery within this group of several members which exert a "physiological" influence on their host has led to exhaustive studies of the hormone content of these ovarian neoplasms. Experimental production of ovarian tumors, while confined to observations on animals, has opened up an entirely new field for investigating some fundamental histogenetic problems, the solutions of which for years have, in human beings, defied the efforts of embryologists and pathologists alike. With this rapid expansion of knowledge a review from time to time is necessary in order to evaluate certain current facts which have been established in these different lines of endeavor. The present review is an attempt to correlate data which have recently accumulated on the subject of ovarian neoplasms. It covers the literature for a six-year period beginning July, 1938, and embodies information from more than 400 articles, some 200 of which appear as pertinent bibliographic references. All of these references were consulted in the original form except in the case of those in which the journal was not available but in which a satisfactory abstract had been made elsewhere. I shall attempt to give an account of my "digest" without personal bias and with the hope that my errors of omission and commission will not be judged too unkindly.

CLASSIFICATION OF OVARIAN NEOPLASMS

It is highly desirable in classifying neoplasms of a given organ to be able to trace the development of the new growths therein developing to different cellular prototypes which are normally located within that organ. In attempting to apply this principle to the classification of ovarian neoplasms one is at once confronted with the difficulty that there are many more tumors than there are tissue types. Fortunately, however, the complex development of the ovary permits (or invites) the inclusion of adjacent structural elements on the one hand and the developmental arrest of native tissue elements on the other, which affords an added latitude of interpretation. Of several recently advanced proposals for a histogenetically reasonable grouping of these tumors the one of Schiller (2) will serve as a model.

A. Ovarigenic. Derived from ovarian tissues
   1. Granulosa-cell tumor
   2. Fibroma (simple and luteinized)
   3. Myxoma, angioma, luteinoma

B. Heterotopic. Derived from tissues not normally present within the ovary
   1. By pathological differentiation
      a. From surface mantle via prosoplasia in direction of muellerian epithelium
         (1) Serous cystoma and derivatives (tubal type of epithelium)
         (2) Endometrioma (uterine fundal type of epithelium)
         (3) Mucinous cystadenoma including malignant variants (uterine cervical type of epithelium)
      b. From mesenchymal (ovarian) core by error in sex chromosomes
         (1) Arrhenoblastoma (from male-directed elements)
         (2) Dysgerminoma (from neutral or dysgerminal elements)
   2. From "accessory" tissues (displaced)
      a. In fetal life

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(1) Early—teratomas, mature (dermoids) and immature (embryomas)
(2) Late—from tissues in vicinity of ovary—ganglioneuroma, mesonephroma, hypernephroma, Brenner tumor (urogenital epithelium)

b. In adult life
(1) By implantation (endometrioma)
(2) By metastasis (Krukenberg's tumors and allied neoplasms)

A modification of Schiller's classification is that of Meigs (1), who favors augmenting the "mesenchymal" group by the inclusion of granulosa-cell tumors, theca-cell tumors, fibromas, and sarcomas. In addition, Meigs derives teratomas from parthenogenetically divided ova instead of placing them in the group arising from "displaced" elements.

The classification of Taylor (3), based for the most part on histological interpretation, has much to recommend it. He divides ovarian tumors according to the following scheme:

A. Functional cysts (corpus luteum, follicular, and so forth)
B. Endometrial cysts
C. True neoplasms
1. Common epithelial neoplasms
a. Serous cystadenoma and derivatives
b. Mucinous cystadenoma and derivatives
2. Connective-tissue tumors—fibroma, sarcoma, theca-cell tumor, and so forth
3. Mixed tumors—dermoids and more complex teratomas
4. Parenchymal tumors—granulosa-cell tumor, arrhenoblastoma, dysgerminoma
5. Tumors of uncertain status—Brenner tumor, hypernephroma, mesonephroma
D. Metastatic tumors

Taylor's exclusion of endometriomas from the family of ovarian neoplasms is based on the observation that they frequently occur as primary growths in locations other than ovarian and the fact that their origin has not been entirely agreed on. In common with Schiller, Meigs, and other investigators, Taylor no longer looks on simple cysts as being of a neoplastic nature.

The aforementioned three classifications serve only as samples; every pathologist seems to cherish his own. For the purposes of the present review I shall delete consideration of the endometriomas for the reason cited in the preceding paragraph.

For the true neoplasms, I shall herein attempt no new classification but rather discuss individual types, and hope that the reader can fit them into some practical working scheme.

SEROUS CYSTADENOMA (SEROUS CYSTOMA, OVARIAN ENDOSALPINGIOMA, AND SO FORTH)

Under this heading are included one main group of cystic tumors and a miscellany of semisolid and solid variants which Barzilai (1), Geist (4), and others have found listed throughout the literature under no less than 20 different titles. The common denominator is the existence of epithelial cells which, although columnar, are not mucus-producing and which are not associated with a stroma characteristic of ovarian endometriosis.

Histogenetically, present-day concepts derive these tumors from a muellerian type of epithelium. There still remains the matter of dispute as to whether this epithelium originates from the so-called germinal epithelial mantle by a process of metaplasia or whether anatomic rests of tubal lining play the predominating role. Whereas it was formerly thought that the "germinal epithelium" through the medium of Pflueger's tubules was the source of serous cystadenoma, the recent work of Fischel (3) has shown that these tubules do not exist in the human ovary. In spite of this evidence, which tends to discount the multipotency formerly ascribed to the germinal epithelium, the majority of pathologists, including Meyer (9), regard this layer as the source for this and, indeed, for other ovarian neoplasms. Schiller (12) and Barzilai (1) lead the list of investigators who believe that the epithelial elements of these tumors are of definitely tubal origin. Barzilai, in proposing the histogenetically suggestive term "endosalpingioma" for this group of ovarian neoplasms, presents an array of convincing evidence in favor of her hypothesis. In the microscopic study of her tumors she found four types of epithelial cells which were characteristic of tubal lining and she also observed cyclical changes in these cells paralleling those observed in the tube during the various phases of the menstrual cycle, and attending the menopause. Everyone interested in this phase of the subject should study Barzilai's chapter on endosalpingioma of the ovary. An origin from wolffian remnants and the "old reliable" notion of teratomatous development have not been invoked in explaining the histogenesis of serous cystadenoma.

Clinically, these tumors comprise about 15 per cent of ovarian neoplasms, being somewhat less frequent than mucinous cysts. They are not observed prior to puberty and affect, for the most part, women between the ages of twenty and fifty years. The symptoms are of the same nonspecific nature as those recorded for mucinous cystadenoma, except that sterility is more fre-

quent (25 per cent) and ascites is encountered commonly. Traumatic and spontaneous ruptures (Spring, 14) occasionally occur and along with twisting of the tumor pedicles (6) may give rise to signs indicative of an acute condition within the abdomen (Hardt and Seed, 5).

Grossly, at operation the tumors are found to be from moderate to large in size. They are bilateral in perhaps 30 per cent of the entire group and in 50 per cent of the papillary examples. The majority will be unilocular and completely cystic, but mulberry and solid types are sometimes encountered. Papillary projections are seen much more frequently than with mucinous cystadenomas and when they are present they are found with both the inverting and everting gross patterns. Those growths which exhibit soft cauliflower projections on the outer surfaces of the cysts are oftentimes associated with widespread peritoneal dissemination of "implants" and with abdominal ascites. In other instances in which the papillary projections are hard, white, and mulberry-like, no ascitic fluid is usually present and the peritoneal surfaces of the surrounding viscera are smooth. In still other instances solid growths involving one or both ovaries will lead to the mistaken diagnosis of ovarian fibroma. These fibrous varieties chiefly affect older patients (Scott, 13; Barzilai, 1).

Microscopically, the group may be conveniently divided into papillary and nonpapillary types, with the former in marked predominance. In both groups, according to Barzilai (1), one can identify cells of the following characteristics:

1. Secretory (nonciliated) epithelial cells which may be columnar, pear-shaped, prismatic, or cuboidal. The nuclei of these cells are basally placed, oval in outline, and oriented in lines parallel to the long axes of the cells. These duplicate in appearance the secretory cells of the fallopian tube, and the variations in their structure are apparently based on a comparable hormonal response. In tumors removed from older women these cells are nearly all cuboidal.

2. Tall, ciliated cells with clear cytoplasm and oval nuclei located near the ciliated border and oriented at right angles to the long axis of the cells.

3. Intercalary, or peg, cells which are long and slender and which are almost devoid of cytoplasm. The nuclei of these cells are small and their axes variable.

4. Occasional large round vesicular cells with transparent cytoplasm and dark round nuclei.

The appearance and the orientation of these cells appear to be very much like the arrangement seen in the tubal mucosa. The cells rest on a sharply defined basement membrane of fibrous composition. Among papillary examples of the neoplasm the connective cores may be (1) thin and delicate, (2) voluminous and filled with edema fluid, or (3) very thick and so hyalinized that the microscopic appearance of individual units suggests fibromatous structures covered by single layers of atrophic-appearing and dark-staining cuboidal cells. According to Barzilai (1) the truly fibrous variants are seen in older women, whereas in younger women suffering from the effects of these neoplasms there is much more luxuriant epithelial proliferation and a much less fibrous connective-tissue support. Multiplication of the epithelial layers is supposed to occur infrequently, although fusion of adjacent "villi" and tangential microscopic sections may simulate the appearance of stratification. Mitoses are rare; calcification may be present; metaplasia to squamous epithelium has been observed (Geist, 4). Ovarian adenofibromas with or without papillary features probably represent a variant of this neoplasm.

The microscopic evaluation of malignancy in this group of tumors has been the subject of debate for years. In general, the cystic, nonpapillary, and the solid, adenofibromatous examples nearly always prove to be benign clinically and pathologically. The same may be said for the hard, white, warty variant of the papillary cystadenoma. However, anything but universal agreement exists concerning reports on the soft, luxuriant, villous-like growths which are so often bilateral and so frequently associated with peritoneal implants. Ewing (2) classifies these tumors as being of a low order of malignancy, observing that they frequently terminate fatally and that, in addition to their tendency toward peritoneal implantation, they occasionally metastasize to the abdominal lymph nodes and even distant organs. He admits, on the other hand, that spontaneous regression occasionally occurs. It has been observed by many (Morton, 10; Taylor, 15; Meigs, 8; MacCarty, 7; Geist, 4) that operative removal of both involved ovaries is sometimes followed by disappearance of the peritoneal "seedlings," and it is quite possible that the maintenance of this metastasis may be related to an ovarian hormonal influence comparable to the relation of testicular hormones to the cells in a prostatic carcinoma. Geist (4) believes that 80 per cent of these papillary tumors are of a low order of malignancy, but paradoxically states that purely benign forms may recur and metastasize. Taylor (15) regards them in the light of semimalignant tumors. Barzilai (1) classifies her "endosalpingiomas" in the benign category but admits that some may be-

come malignant. She is inclined to regard peritoneal metastasis in the light of "muellerian potentialities," comparable to peritoneal involvement in endometriosis. Novak (11) recognizes the difficulty of separating benign from malignant examples microscopically but feels that stratification of epithelial cells, the presence of degrees of anaplasia with mitoses, and evidence of invasion of the stroma are indicative of rapid growth. He observes that when these papillary growths are frankly benign histologically, the clinical course is favorable with certain exceptions. When, on the other hand, the tumor is histologically malignant the clinical course is also a "malignant" one.

The treatment of serous cystadenomas consists of surgical removal of the involved ovary or ovaries, care being taken not to contaminate the peritoneum with the cyst contents, which occasionally contain malignant cells. For the obviously fibrous papillary type in the absence of peritoneal seeding, similar treatment is applicable in younger women, but in the older age group hysterectomy along with bilateral salpingo-oophorectomy is recommended. For the luxuriant papillary growths which are unilateral and entirely intracystic, unilateral salpingo-oophorectomy will probably suffice if the patient is young. Again, if the patient is a young woman with bilateral tumors of markedly disproportionate size the surgeon may find it necessary for various reasons to attempt conservation of the uterus and a portion of one ovary. This is a difficult decision and one fraught with the danger of possible recurrence of the neoplasm. Extracystic tumors even without obvious metastasis should be dealt with radically. Finally, in cases in which the lesions are large and when multiple superficial peritoneal implants of a fine feathery character are present, a surgical "miracle" can occasionally be accomplished by the surgeon who can effect removal of the primary tumors along with the tubes and uterus.

In this latter group of cases Geist (4) advises leaving the cervix behind to serve as a portal for postoperative therapy with radium. Therapy with roentgen rays should also be carried out in all cases in which the tumor is clinically or histologically malignant and in which there is any evidence of extracystic growth.

PSEUDOMUCINOUS CYSTADENOMA (MUCINOUS CYSTADENOMA)

The histogenetic interpretation of this tumor, composed as it is of cells which have no counterpart in the normal ovary, is that it is derived from extraneous elements, and various tissues have been accused of being the "source of supply." As pointed out by Barzilai (1), the uterine cervix and the colonic mucosa alone in adult life contain cells similar to those of the mucinous cystadenoma. The wolffian duct during embryonic life furnishes us with a third possible cellular prototype. Accordingly, we find Novak (8) following along with Meyer (7) in deriving the neoplasm from teratomas by way of an overgrowth of entodermic epithelium. Salient possible facts in the evidence favoring this view might be listed as: (1) the frequent occurrence of mucinous cysts in the walls of ovarian dermoids, and vice versa; (2) the demonstration in tumors of this type of intestinal enzymes such as invertase (Tachibana, 11); (3) the occurrence in cases of peritoneal myxoma of microscopically identical lesions in the ovary and in the appendix; (4) the known tendency for the predominance of one tissue type in ovarian teratomas as illustrated by the condition known as struma ovarii; and (5) the observation by Schiller (10) that pseudomucin is merely "old" mucin and not a substance peculiar to ovarian tumors.

The "muellerian" hypothesis of origin suggested by Schiller (10) in his recent classification has for its basis the similarity of the epithelial lining of mucinous ovarian cysts to the lining of the cervical canal. Whether the underlying mechanism involves metaplasia from germinal epithelium or the presence of actual muellerian rests, the result is the same. Schiller pointed to the ciliated cells of serous cystadenomas, the endometrial-like cells of ovarian endometriosis, and the mucous cells of mucinous cystadenoma as representing the three types of cells lining the tubes, uterine fundus, and uterine cervix, respectively. On the surface, this hypothesis seems logical. Barzilai (1) recalls the occasional appearance of ciliated epithelium investing the ovary and favors the "metaplastic" interpretation of Schiller's concept.

The "wolffian" hypothesis of histogenesis is discussed later under the heading of Brenner tumor. Pseudomucinous cystadenoma comes into this hypothesis rather naturally because about 30 per cent of the Brenner tumors occur in the form of solid nodules located in the walls of mucinous cysts. Several investigators, including Schiller and Novak (8), feel that the "Brenner" portion of this strange combination may secondarily give rise to the larger mucinous portion. Others would reverse the interpretation and regard the Brenner tumor as further evidence favoring the hypothesis of teratomatous origin.

Clinically, mucinous cystadenoma constitutes from 20 to 30 per cent of ovarian neoplasms. The tumors practically never occur before the age of puberty and only about 10 per cent affect women

in the postmenopausal years of life. Fertility is apparently not affected; in fact Geist (4) in his series of cases observed that few women with pseudomucinous cysts who were in the childbearing age were childless. Symptoms are not pathognomonic, and although Te Linde (13) and Rickford and Whapham (9) observed postmenopausal bleeding associated with the presence of this tumor, the cause of this symptom has been ascribed to pelvic congestion resulting from partial obstruction of the returning uterine blood flow. It appears doubtful that the small amounts of estrogenic hormone found by Watts and Adair (14) in cysts of the mucinous type could exert any profound physiological effect on the endometrium. Moreover, the majority of investigators express surprise that menstrual function can be continued in so many cases wherein bilateral mucinous cystadenomas seem to destroy almost every vestige of ovarian tissue. Torsion of the tumor with its attendant symptoms is a feature in perhaps 20 per cent of the cases (Hardt and Seed, 5; Geist, 4).

At operation the tumors are unilateral in about 80 per cent of the cases, of an average large size, and adherent or parasitic in about one-fifth of the cases (6). Most commonly they are completely cystic and multilocular, but some of the "parvilocular" examples may be solid or semisolid. Papillary projections, occurring in 10 per cent, are intracystic, as pointed out by Geist (4), and are strongly suggestive of malignant change. Rupture occurs in only about 5 per cent and in certain cases is accompanied occasionally by the condition of peritoneal myxoma discussed subsequently. In these latter cases the appendix may be the seat of a mucocele or a mucinous carcinoma. Ascites and even hydrothorax may be present, even in the absence of rupture or of myxomatous peritonitis. Dermoid cysts are associated in approximately 10 per cent, and solid Brenner tumor nodules are occasionally found in the walls.

The microscopic picture of large and small cysts with well differentiated goblet cells showing basally placed, crescent-shaped nuclei lying in single rows on sharply defined basement membranes is too well known to merit detailed description. Furthermore, the odd 5 per cent of these tumors that are manifestly malignant will be discussed in the section dealing with ovarian carcinoma. Of present concern is the group comprising perhaps 10 per cent which show papillary projections within the cyst walls and which occasionally produce peritoneal myxoma. This group lies in the "twilight" zone between the frankly benign and the frankly malignant examples. Most investigators, including Novak (8) and Geist (4), regard this group as clinically malignant and observe a more than 50 per cent mortality rate from late recurrence, intestinal obstruction, and even metastasis. From the histological standpoint opinions vary, with Barzilai (1) stating that the microscopic picture is benign, Taylor (12) referring to it as being semimalignant, and Woodruff and McDonald (15), who consider the appendical counterpart of this neoplasm, pronouncing them all malignant. Geist (4) seems to lean toward the last-mentioned view when he states that 80 per cent of his papillary mucinous cysts were malignant. Ewing (3), too, recognizes benign and malignant types of peritoneal myxoma.

The whole picture is complicated by reports of what were originally described as nonpapillary mucinous cysts recurring with peritoneal myxoma, and, on the other hand, certain cases of the latter which cleared up spontaneously. Perhaps the solution will be forthcoming with repetition of the experiments of Zondek and others (16), who successfully transplanted into mice the material from a case of human peritoneal pseudomyxoma. The material proliferated and formed tumors. These authors cite unsuccessful attempts by others to duplicate the mouse lesions using the contents of benign mucinous cysts of the ovary.

In young women the treatment of mucinous cystadenomas consists of removal of the affected ovary and a careful watch for the appearance of a similar tumor on the other side. Because of the possibility of intracystic regions of a malignant nature it is suggested by Novak that evacuation of the cyst contents at operation should be avoided, as the risk of spilling, even through a trocar wound, is great. In other words, the price of a short incision may be a subsequent recurrence in the scar or peritoneal dissemination of cancer cells. In older women suffering from tumors of this type the need for conservatism is not great, but, regardless of age, the operation should be radical when malignant tissue is found. Some women who have peritoneal myxoma may live for years after removal of the pelvic organs along with as much of the mucoid material as is consistent with surgical safety. The appendix should not be forgotten in these cases (2). Roentgen rays may prolong life in those instances wherein surgical extirpation of the lesion was accomplished with questionable completeness.

CARCINOMA OF THE OVARY

Although a certain number of ovarian neoplasms which were formerly described as ovarian carcinomas have recently been segregated as being examples of granulosa-cell tumor, mesonephroma,

dysgerminoma, and so forth, the residuum comprises one of the largest groups of ovarian tumors. Within the group as a whole there appear to be a number of special types, regarding the classification of which there exists no unanimity of opinion. Furthermore, as pointed out previously, the dividing line between benign and malignant examples of papillary growths is by no means sharp, and as a consequence the reports on incidence, symptomatology, treatment, and prognosis are sometimes influenced by the author's conception of what actually constitutes a primary ovarian carcinoma.

In the matter of histogenesis Barzilai (1, 2) recognizes one type which she terms seroanaplastic carcinoma of the ovary and which she believes is of definitely muellerian (tubal) origin. In some instances she believes that it develops from a preexisting benign counterpart, the endosalpingioma; in others directly as a malignant tumor from tubal epithelial rests or via metaplasia of the germinal epithelial mantle of the ovary. Her second type she classifies as a pseudomucinous adenocarcinoma and she considers its origin to be identical in nature with that outlined previously for the mucinous cysts.

Ewing (6) accepted the hypothesis of misplaced "muellerian" epithelium for the histogenesis of ovarian carcinoma, feeling that metaplasia accounted for the mucinous group. He believed that these misplaced "rests" occur in the germinal epithelial layer and that the normal cells of this mantle are not implicated in initiating the malignant process. He recognized serous, mucinous, and intermediate varieties, further subdividing each into cystic and solid, papillary and nonpapillary subgroups. Novak (17) subscribes to Ewing's classification and holds the view that many carcinomas begin in benign cystadenomas, a concept doubted by Goodall (9) and by Meyer. Meigs (14, 16) accepts the germinal-epithelial hypothesis of origin, and suggests metaplasia to endometrial-like tissue in his classification of the neoplasms into pseudomucinous, endometrial-like, and miscellaneous groups. He points out that, like true endometrial carcinoma, the second type appears to grow rather slowly until the capsule is breached and then it spreads with unusual rapidity. He attributes the regression of papillary peritoneal implants following bilateral oophorectomy to the removal of the source of estrogen production, a production which may sustain the proliferation of these "secondaries." (This interesting speculation has a parallel in the temporary regression of the metastasis from prostatic carcinoma following removal of the testes.) Although an origin in ovarian endometriosis would seem logical, no one has satisfactorily demonstrated the stages of such a transition. Rewell's (20) instance of a primary ovarian adenoacanthoma, along with 3 comparable examples in the literature, presents a marked microscopic similarity to the well-known condition of uterine adenoacanthoma. However, histogenetic interpretations based on histological similarity are notoriously unreliable and one should never forget that adenoacanthomas can arise in locations like the gall bladder in which the lining cells are definitely of nonmuellerian ancestry.

Clinically it is difficult to estimate the incidence of primary ovarian carcinoma inasmuch as different investigators utilize different criteria for diagnosis, especially of the papillary group of neoplasms. Barzilai (1, 2) estimates that 15 per cent of ovarian neoplasms are seroanaplastic carcinomas and that 6 per cent are pseudomucinous adenocarcinomas. Shands and Clark (27) found that among patients less than forty years of age 2.7 per cent of the ovarian tumors were malignant —a figure which reached 14.3 per cent in the forty- to fifty-year age bracket—and that among patients more than fifty years of age 69 per cent of the ovarian neoplasms were malignant. Goldsmith (8), in a very large series, found that 2.6 per cent of his patients suffering from gynecologic conditions had ovarian neoplasms. Of these tumors, 24 per cent were malignant. The incidence of malignant lesions increased from 24 to 70 per cent when only the postmenopausal group was considered. Marchetti (13) in an extensive experience found that 17 per cent of malignant gynecologic neoplasms were ovarian carcinomas. Of these, 73 per cent were serous cystadenocarcinomas, 10 per cent were pseudomucinous adenocarcinomas, and the remainder were malignant teratomas, and so forth. From these and other articles on the subject it can be gathered that ovarian carcinoma of this type is fairly common, that it is practically never observed in children and is rare among women less than thirty years of age, and that, once the menopause has been reached, the likelihood that an ovarian neoplasm is malignant is more than 50 per cent. Seroanaplastic carcinomas are encountered from four to six times as frequently as pseudomucinous adenocarcinomas.

In the matter of symptomatology all authorities agree with Crossen (5), with Scheffey (25), and with Meigs (16) that ovarian carcinoma in its early stages is a "silent menace." Pelviabdominal pain, a common early symptom of the condition, often heralds the stage of ineradicable extension, as pointed out by Goodall (9). This pain is de-

scribed as resulting from peritoneal irritation from implants, pressure on the neighboring viscera (bladder) and invasion of the nerves, acute torsion (10 per cent, Geist [7]; 3 per cent, Keith [11]), and intestinal obstruction in the approximately 50 per cent of these tumors which terminally tend to involve the colon or the small intestine (Jones, 10). Among 152 patients in Geist's series, 13 were admitted to the hospital suffering from pain characteristic of intestinal obstruction. Abdominal enlargement either from ascites or from expansion of the tumor is noted in more than 50 per cent (Marchetti, 13), and the diagnosis of carcinoma can at times be made from examination of ascitic fluid withdrawn by paracentesis (Meigs, 16; Jones, 10). In 30 per cent of Meigs's series (15) abnormal vaginal bleeding was a symptom, and postmenopausal "spotting" was a feature in 10 per cent of his postmenopausal group of patients. Geist (7) observed, on the other hand, that menstrual abnormalities were infrequently associated with primary ovarian carcinoma of the papillary type, but he cited a marked difference of opinion as to the incidence of this symptom. In some cases abnormal bleeding is due to the presence of uterine metastasis (Lynch and Dockerty, 12; Pemberton, 18); in others, to pelvic congestion, and in still others, to such conditions as uterine leiomyoma, polyps, benign endometrial hyperplasia, and so forth. Interestingly enough the symptom may in some way be related to a 40 per cent incidence of sterility which has been observed among patients suffering from the effects of ovarian carcinoma. Meigs (16), commenting on the symptom of sterility, wondered whether the ovaries engendering these neoplasms were not in fact congenitally defective. Bossert (4), on the other hand, was able to find reports on 14 malignant ovarian tumors occurring concomitantly with pregnancy.

When the neoplasms are observed grossly at the time of operation, decision as to whether they are benign or malignant cannot always be made. This is true especially in those instances wherein the growth is confined to the inner wall of a cyst. Those of an obviously malignant nature may, however, be conveniently grouped into certain categories with a view toward the planning of subsequent treatment. As pointed out by Meigs (15), Barzilai (1, 2), and others, they may be unilateral or bilateral, solid or cystic, but they are completely encapsulated (completely removable). They may be grossly papillary and "exfoliating," with or without pelvic implants (probably removable). With the features previously mentioned, they may demonstrate extensive omental and peritoneal "implants" of a superficial character (probably not all removable), on the one hand, and omental "caking" of a massive nature with nodal and other metastasis (inoperable). Bilaterality is a very common (80+ per cent) feature with solid neoplasms of this type and with grossly papillary lesions. In both instances ascites is present in more than 50 per cent of the cases (Geist, 7 and Meigs, 15), and frequently the fluid is hemorrhagic. Marchetti (13) found concomitant hydrothorax in 13 per cent of his series. Adhesions are frequent. Peritoneal pseudomyxoma is observed occasionally.

Microscopically, Barzilai (1, 2) has given the best description of the variegated picture presented by these neoplasms and her work should be consulted by all those interested. Briefly, in the seroanaplastic group she finds pure and mixed pictures of cells which may be basically small dark cells, large clear cells, and wild syncytial-like, anaplastic cells. Arrangement of these cells occurs in all patterns from the orderly papillary architecture of some of the less malignant examples through adenopapillary, alveolar, to medullary and diffuse patterns in which cellular differentiation may not be apparent. In her pseudomucinous variety the basic mucin-producing cellular elements demonstrate comparable shades of differentiation and anaplasia but usually with preservation of some degree of glandlike formation. Among specimens of both types the connective tissue has varied in amount and in quality, presenting desmoplastic reactions in some and an almost sarcomatous appearance in others. Various investigators, including Taylor and Greeley (29) and Pemberton (18), applying the principle of "grading" to these neoplasms, note that ovarian carcinomas, like carcinomas of the breast and uterine cervix, are of a high order of malignancy in about 80 per cent of the cases. Taylor and Greeley felt that next to the all-important matter of gross extension, grading is the most useful criterion on which to base prognosis in cases of ovarian carcinoma. The "feathery" type of ovarian cystadenocarcinoma appeared to be of the lowest order of malignancy, and a microscopic diagnosis of this particular type occasionally dictated the decision to remove radically a growth which under other circumstances (such as an opinion based on gross appearance) would have indicated a hopelessly incurable condition (28). In general, the pseudomucinous carcinomas are less malignant histologically than the serous cystadenocarcinomas (Meigs).

Treatment. The principal recent changes wrought in the surgical treatment of ovarian car-

cinoma have been brought about, on the one hand, by more radical removal of well differentiated papillary carcinomas which were previously considered inoperable (Meigs, 15; Keith, 11; Pemberton, 18; Jones, 10) and, on the other, by removal of both ovaries in unilateral ovarian carcinoma. Meigs (14) states that the only possible exception to the latter rule is that of the young woman who desires to have children and whose ovarian carcinoma is unilateral and encapsulated. Preservation of the "sound" ovary, while carried out at the surgeon's own risk, may be considered, provided the patient returns every six months for close observation and immediate operation in the event of a "recurrence" of the neoplasm. Hysterectomy with bilateral salpingo-oophorectomy is feasible in about 60 per cent of the cases of ovarian carcinoma. Certain authorities (Walter, Bachman and Harris, 31; and Keith, 11) believe it is advantageous to preserve the uterine cervix as a portal for the subsequent employment of roentgen rays. Others (Ramsey, 19 and Meigs, 16) feel that this is not a matter of consequence. Pemberton (18) recommends removal of omental metastasis while Meigs is of the opinion that this procedure is useful only in those cases in which the omentum contains the only secondary deposit. However, superficial implants of a low order of malignancy can be removed with some hope that the remainder will regress following removal of all ovarian tissue. Peritoneoscopy with biopsy is a minor procedure which in many cases has established a diagnosis and in some cases has obviated the necessity for laparotomy with its attendant mortality rate of from 5 to 10 per cent in ovarian carcinoma. Abdominal paracentesis, in addition to being a diagnostic procedure, has therapeutic value in enhancing the effect of roentgen therapy for these neoplasms (Schmitz, 26).

Conflicting as are the opinions regarding the efficacy of roentgen therapy, one cannot escape the conviction that the recent improvement in the "survival statistics" for patients with ovarian carcinoma is in large part due to this form of treatment. Apparent "cures" resulting from such roentgen therapy are recorded by Jones (10), and Shands and Clark (27). Pemberton (18), Shands and Clark, and Keith (11) believe that roentgen therapy alone or as an adjunct to surgical operation prolongs life, reduces ascites formation, and makes more comfortable the lives of patients who suffer from this form of cancer. They warn, however, against too vigorous "irradiation" in old and debilitated subjects as well as in those in the late stages of emaciation. The modern large "dosages" advocated consist of approximately 2,000 roentgens delivered through each of from four to six portals by methods which have been well outlined by Marchetti (13) and by Keith (11). Goodall (9) and Meigs (16), on the other hand, are of the opinion that roentgen therapy in no way alters the prognosis in cases of ovarian carcinoma. Traut (30), taking a more conservative view, feels that mucinous adenocarcinomas and the more differentiated examples of papillary ovarian carcinoma are definitely "radioresistant." Taylor, while observing that advances in the roentgen therapy of ovarian carcinoma "remain more of a promise than a reality," admits that improvement in the end-results has accrued from this form of treatment. He stresses the need for meticulous correlation of the histological types of ovarian carcinoma with the response of these types to therapy with roentgen rays and he believes that benefits to patients will accrue from such a study. Walter, Bachman, and Harris (31) discuss the ways and means of preventing "irradiation sickness" so commonly observed.

Therapy based on the principle that the administration of androgenic substances might inhibit the growth of ovarian carcinoma cells gave discouraging results in the hands of Beecham (3).

The prognosis in cases of ovarian carcinoma is gloomy in all save the differentiated types of tumors, which comprise only about 20 per cent of the total. As mentioned previously, in approximately 40 per cent of the cases these are irremovable masses. Bilateral ovarian involvement with solid neoplasms makes up 10 per cent of the remainder and carries an initial five-year mortality rate of almost 80 per cent. Pelvic adhesions, nodular infiltrations of the surrounding viscera, omental "caking," malignant ascites, and distant metastasis are serious features which have been outlined in the foregoing paragraphs and which affect the outlook adversely. Even with fairly "adequate" treatment Pemberton (18) reports a five-year survival rate of only 39 per cent (or 27 per cent of his entire series). Meigs (15), in a comparable analysis, finds only a 15 per cent salvage of patients. Taylor, similarly, records surgical "cures" in 15 per cent only. In a recent, although smaller, series, Taylor found that the combination of radical surgical measures with postoperative roentgen therapy gave five-year survivals in 35 per cent of the cases. The majority of the cures were obtained in the group of more highly differentiated histological types.

Certain other miscellaneous ovarian neoplasms have been reported which do not properly belong in the discussion of ovarian carcinoma but which are recorded here for the sake of brevity. Rice,

Pearson, and Treadwell (21) record a case of malignant ovarian lymphangioma of rapidly fatal evolution, death occurring in eight months from metastasis. They were able to find in the literature only 3 instances of a similar type of tumor. Schaeffer and Cancelmo (24) observed a cavernous hemangioma involving the right ovary of a twelve-year-old girl. They found 3 similar cases in the literature. The "myeloid tumor of the ovaries" reported by Sammartino and Herrera (23) is difficult to interpret inasmuch as many other organs were infiltrated by tumor cells of the myeloid series. The ovarian neoplasms probably were metastatic. Other tumors like the one reported by Sager (22) probably represent atypical neoplasia occurring in ovarian teratomas. Especially is this suspicion justified when these tumors are found in children. No definite rules can be formulated for the treatment of this miscellaneous group, each case being a law unto itself and the disposition thereof depending on whether the neoplasm is benign or malignant.

OVARIAN FIBROMAS

In 1944 Masson and I (6) reviewed the literature on ovarian fibromas and presented a clinical and pathological analysis of a large series of cases. The following notations represent a somewhat abbreviated summary of this and other papers concerning a tumor which, after receiving desultory attention for 200 years, has finally "come into its own," so to speak.

Results of studies on histogenesis have, so far, not improved on the hypothesis of Coe (4), who believed that ovarian fibromas represent an overgrowth of the ovarian cortical stroma, and that of Brothers (3), who believed that this overgrowth is in the nature of a keloid response to hemorrhage within the ovary. Although the absence of ovarian fibromas before the age of puberty might point to the presence of hormonal influence, the inability to duplicate in the ovary the estrogen-induced uterine "fibroids" experimentally argues against such a causal mechanism.

While these tumors may develop clinically, at any time after the onset of puberty, they rarely produce symptoms until they become large enough to rise out of the true pelvis. Complaints of the patients are for the most part non-specific and related to the disturbed intra-abdominal mechanics attendant on the presence of any slowly growing pelvic tumor. One notable exception to this rule is afforded by the production of ascites, usually large in amount, which is present in almost 40 per cent of the cases in which the tumors measure 6 cm. in diameter or more. In from 2 to 3 per cent of these cases exhibiting ascites, hydrothorax is also present, completing a group of clinical phenomena generally known as Meigs' syndrome (1).

For many years the occurrence of ascites (to say nothing of hydrothorax) with pelvic tumors had been tantamount to making a diagnosis of "inoperable neoplasm," and undoubtedly many patients with ovarian fibroma had been denied the benefits of curative surgical procedures on this basis. The contributions of Meigs and his coworkers in these "salvage operations" cannot be overemphasized.

Since they first began their work in 1937 these investigators have reviewed cases from the older literature (Cullingworth, 5; Tait, 16; and Hoon, 9) and added a number of cases they had personally studied (12, 13). In 1943 they correlated the clinical and pathological data on some 27 cases—a number which has been swelled to well over 30 by other contributors (Herrick, Tyson, and Watson, 8; Thompson, 17; Dockerty and Masson, 6; Gild, 7; Bomze and Kirshbaum, 2). So awakened became the interest in the subject that gynecologists began reporting examples of granulosa-cell tumor (18), theca-cell tumor (14), Brenner tumor (10), and so forth (5, 11, 15), associated with ascites and hydrothorax, thus demonstrating that the ability to produce the syndrome was not something inherent in the cells of ovarian fibroma. The causation of the ascitic fluid is generally ascribed to venous obstruction within the tumor consequent to twisting and untwisting of the tumor pedicle. The relationship of the abdominal to the thoracic fluid was a complete mystery until solved by the brilliant experiments of Megis, Armstrong, and Hamilton (13) in which particulate matter (India ink) was used to demonstrate that the thoracic fluid was of abdominal origin. The particles which they injected intraperitoneally in their cases appeared later within the thorax. Carriage by means of phagocytes circulating in the blood was ruled out by examination of the "buffy coat" of a centrifuged blood sample. Collateral experiments showed that transdiaphragmatic carriage of fluid containing the particles apparently did not occur in the reverse direction, namely, from thorax to abdomen. The influence of negative intrathoracic pressure (especially as related to the high incidence of right versus left and bilateral hydrothorax), existence of pleuroperitoneal "pores" or lymphatics as possible conduits for the passage of fluid, and the rarity of the ascites-hydrothorax combination in hepatic cirrhosis are related problems which are at present under investigation.

At surgical exploration ovarian fibroma is a solid or solid-cystic, lobulated, encapsulated, hard grayish-white tumor, unilateral in about 90 per cent of the cases and in general easily recognized as such. The appearance of bilateral fibromalike ovarian lesions should suggest the possibility of Krukenberg tumor and a search should be carried out for the primary growth in the upper part of the abdomen. Dark, soft zones are unusual in ovarian fibromas but when present are sometimes indicative of sarcomatous change and dictate radical operative procedures for a tumor which otherwise responds well to local removal.

Pathologically, fibrous and cellular types constitute the picture of this neoplasm, whose units are modified ovarian cortical stromal cells (fibroblasts) arranged in a close "featherstitch" pattern. The cellular architecture may lead one into the pitfall of labeling a number of these tumors as fibrosarcomas. However, regardless of cellularity, the absence of mitotic figures in all but 2 per cent of ovarian fibromas substantiates a diagnosis of benign neoplasm, which is borne out by the subsequent clinical course of the patient. A certain number of so-called fibromas showing fatty change (with or without calcification) will prove on analysis to represent theca-cell tumor; others will be reclassified as Brenner tumors; the gross difficulty of differentiating fibroma from Krukenberg tumor is carried over into the microscopic examination if one does not remember that "signet-ring cells" are never native to an ovarian fibroma.

DERMOID CYSTS AND COMPLEX TERATOMAS

The older conception that a dermoid cyst of the ovary was but a ball of hair surrounded by a layer of ectodermal tissue has undergone extensive revision in recent times. Repeated studies have amply shown that far from being ectodermal tumors, dermoids in most instances reveal tissues from all three germinal layers. Earlier hypotheses of histogenesis which ascribed the origin of these tumors to nightmares, sexual relations with the devil, witchcraft, divine visitations, and so forth have largely been replaced by the more logical and better documented hypotheses of cellular rests, blastomeric isolation and, more recently, of parthenogenetic development of ova. This last mentioned phenomenon has repeatedly been demonstrated among certain of the lower animals (guinea pig and frog), but has never been actually proved to have occurred within the human ovary. On the other hand, within the testis of the rooster, tumors comparable to human ovarian dermoids have been successfully produced by the use of zinc chloride and zinc sulfate (Michalowsky, 18; Bagg, 3; Falin, 11; Falin and Gromzewa, 12). The origin of these tumors seemed best explained by the hypothesis of parthenogenetic development. Sexual hormones in experimental birds seemed to be positively related to the incidence of tumor formation, and we have a parallel observation in the ovarian dermoids of human beings which in 85 per cent of the cases appeared to arise during the period of sexual activity. Just why these parthenogenetically divided ova do not more frequently develop within the fallopian tube (there are only a few cases in the literature) is one of the problems that await further investigation. Proponents of the hypothesis will also have trouble explaining the occurrence of benign and malignant teratomas in young girls, provided that the tumor is "the offspring and not the brother of the host," as Ewing (10) remarked. Hereditary influences are discussed by Edmonds and Hawkins (9).

From the clinical standpoint it has been pointed out that ovarian dermoids are not present at birth; that during infancy and childhood they are somewhat rare and often more complex in composition with a high ratio of malignant change (Smiley and Auster, 27; Smeltzer, 26); that a relatively high incidence (85 per cent) is seen during the period of sexual activity; and that there is an absence of proved cases in which the tumor had its inception following the menopausal years.

A negative influence of the tumors on ovarian hormonal economy is indicated by an 88 per cent incidence of associated fertility (Blackwell, 4) and by an accumulated series of 50 cases in which bilateral dermoid cysts of the ovary have complicated pregnancy (Doyle and Daversa, 8; Goodwin, 15; Southward, 28; Andrews, Nicholls, and Nicholls, 1; Bowles, 5). The fact that bilateral oophorectomy in these cases is unusually well tolerated by the fetus indicates that the ability of the normal placenta to take over the function of the corpus luteum of pregnancy is apparently not affected by the presence of bilateral ovarian dermoid cysts.

In addition to pregnancy other clinical complications receiving their share of attention have been torsion of the tumor pedicle, which is said to occur in 12 per cent (Piper, 22), and the occasional accident resulting in rupture of the dermoid. Rupture in these cases is a very serious complication leading to a particularly vicious type of granulomatous peritonitis, occasionally with internal (pilimiction) or external fistulas (Piper). In the matter of preoperative diagnosis there has recently been revived (Danelius, 7; Good, 14; Robins and White, 24) a characteristic roentgenolog-

ical sign previously noted by Laurell (16) and Odquist (20). More than 80 per cent of ovarian dermoids are filled with lipoid material which is relatively radiolucent. The thickened dermoid capsule viewed tangentially, as it is in roentgenoscopic examination of the pelvis, appears as a contrastingly radiopaque limiting ring. Application of this "rediscovered" sign should prove valuable in the differential diagnosis of ovarian cysts, especially when one considers the additional roentgenoscopic evidence afforded by the finding of teeth, bones, areas of calcification, and so forth.

One has but to read a standard treatise (for instance, Ewing, 10) in order to get an idea of the pathological heterogenicity of tissues and parts that may be found in ovarian dermoids (28). Some of the later "accessions" might be listed as vertebral-column and notochordal tissue (Riopelle, 23), and the appendix and portion of the ileum (Schottenfeld and Littauer, 25). Recent investigators have concerned themselves more with describing neoplasia of these tissues. In 1939 Stewart, Willis, and De Saram (29) reported the findings in 2 cases of carcinoid tumor arising from the small intestinal portion of ovarian dermoids (28). Gabrilove's carcinoid (13) had a similar origin from gastric tissue. I (unpublished data) have seen a fourth similar case. Blackwell (4) found 1 Brenner tumor in the tissues of an ovarian dermoid. The incidence of mucinous cystadenomas as integral parts of the tumors still stands at about 10 per cent, and epitheliomatous transformation remains at the formerly reported level of 1.5 per cent (Brody, 6). Other neoplastic combinations which more properly belong in the group of solid rather than cystic teratomas are the primary choriomas (17 cases in the literature—Sturley[1], 30; Oda, Matsushita, and Kurosu, 19; Backus and Griffin, 2; Mathieu and Robertson, 17) and carcinomatous and sarcomatous teratomas in which one type of malignant tissue has overgrown most of the remaining elements (Smiley and Auster, 27). Seven primary ovarian melanoepitheliomas fall into this category (Otken, 21). These malignant teratomas, although of the same histogenetic vintage as the ovarian "dermoid" type of cystic teratoma, have a greater tendency to affect women in the prepuberal years of life (Smeltzer, 26).

In the treatment of ovarian dermoids one should never forget the examination of the contralateral ovary. The tumors are bilateral in about 12 per cent of the cases and the experience of "striking oil" in an apparently normal ovary will impress one with the ease of overlooking small tumors of this type. When such small dermoids are encountered they should be shelled out without rupture and the resulting raw surfaces apposed with a minimum of fine suture material. Pregnancy has occasionally ensued after such careful conservation of the ovarian tissue. With large tumors a long incision and an intact capsule will serve the interests of the patient better than a short incision if the latter involves the risk of chronic peritonitis resulting from carelessness in aspirating the highly irritating contents of the cyst. With dermoids complicating early pregnancy, the dictum is to delay operation until the end of the first trimester. In bilateral examples conservation of the corpus luteum of pregnancy is important but not urgent. Dermoids discovered in the last two months of pregnancy can perhaps be watched carefully and removed during an early cesarean section. The treatment of malignancy in dermoids and of malignant solid ovarian teratomas of the types described should follow the principles outlined in the section dealing with primary carcinoma of the ovary.

STRUMAL TUMORS

Strumal tumors (ovarian tumors of thyroid tissue) perhaps have no more right to a separate consideration than do primary ovarian choriomas. However, they do possess signal characteristics of distinction. Formerly variously designated as cystadenomas with colloid degeneration and as metastatic carcinomas from the thyroid gland, the group is now universally recognized as being teratomatous in origin. True colloid-containing thyroid-tissue elements are found in from 1.5 to 28.5 per cent of ovarian dermoid cysts according to the diligence of the "microscopic search" (Cohn and Kushner, 1). Absolute identification of the nature of this thyroid-appearing tissue has been affirmed by chemical (iodine) determinations and by biological experiments on growing tadpoles. In the 150 odd cases in the literature (Sailer, 3) in which thyroid tissue was present in amounts sufficient to justify the designation of strumal tumor, evidence was afforded by the presence of other tissue elements that the tumors were in fact teratomas. In the remaining 20 per cent the thyroid overgrowth was so complete that a teratomatous origin, although accepted, could not be verified microscopically. According to Cohn and Kushner, there is an associated enlargement of the thyroid gland in only about 4 per cent of the cases.

[1]For one to establish a diagnosis of primary ovarian teratomatous chorioma, the association of uterine, tubal, and ovarian pregnancy must be carefully excluded. According to Sturley, of 42 ovarian choriomas in the literature, only 40 per cent appeared to be undoubtedly of teratomatous origin. Of these, 75 per cent were in children. The Ascheim-Zondek test was frequently of diagnostic aid. The prognosis was extremely grave.

From the clinical standpoint the condition is important because a state of hyperthyroidism coexists in more than 5 per cent of the cases (Emge, 2), and without prior knowledge of the type of ovarian tumor, operations are sometimes carried out on the thyroid gland in an effort to make the patient a "better risk for pelvic surgery." Abdominal ascites is frequently present with tumors of this type (Sailer, 3; Emge, 2) and its presence often indicates malignant transformation in the ovarian thyroid tumor.

Pathologically the tumors resemble "nodular goiters" rather than the type of thyroid gland usually associated with exophthalmos. Microscopically one can by no means always correlate the finding of hyperplastic thyroid epithelium with clinical evidence of the hyperthyroid state, and, conversely, one finds the microscopic changes of thyroid activity in tumors that are "physiologically" silent. Results of assaying the tumors for iodine content have likewise failed to reflect significant differences in "active" as opposed to "inactive" strumal tumors.

Adding to these seemingly dissociated observations our present knowledge concerning the role of the thyrotropic pituitary hormone in the production of diffuse thyroid hyperplasia with exophthalmos, one might reasonably doubt the possibility that strumal tumor could exist as a true exophthalmic goiter in the absence of similar changes in the thyroid gland.

Arguing further along these lines we find the high incidence of malignant change involving ovarian strumal tumors correlating well with the known tendency for thyroid adenomas to undergo this transformation, and in contrast with the rarity of carcinoma developing in an exophthalmic goiter. Emge, in a review, found carcinomatous changes in from 5 to 6 per cent of cases of struma ovarii and stated that even with incomplete follow-up data, 50 per cent of these carcinomas eventually proved fatal. Of 9 malignant strumas in the literature only 2 metastasized to distant parts. In the remainder the peritoneal surfaces received the "secondaries" which were usually described as being relatively noninfiltrating. As with ordinary thyroid carcinomas the metastasis sometimes appeared relatively benign microscopically (Wynne, McCartney and McClendon, 4). Removal of secondary deposits could sometimes be repeatedly effected with marked prolongation of the life of the patient (eighteen and one-half years in 1 instance).

One of the most interesting features encountered in the group was the demonstration in 1 case (Emge, 2) that omental metastasis from this type of tumor could in fact give rise to symptoms of thyrotoxicosis. Pronounced improvement of the clinical symptoms and a sharp reduction of the basal metabolic rate followed surgical removal of the metastatic deposits of thyroid tissue.

GRANULOSA-CELL TUMOR

Within the past five years no ovarian tumor has received more attention than this "feminizing" member of the ovarian family. In 1939 the number of reported examples was about 300 but this number has since been doubled. The neoplasm has lent itself to study from a variety of different angles which perhaps merit a somewhat detailed examination.

Furth and Butterworth (12), Traut and Marchetti (43), and later Geist, Gaines, and Pollack (14) succeeded in producing granulosa-cell and theca-cell[1] tumors in mice by irradiation of young and mature animals with roentgen rays. The tumors were biologically active. Histogenetic studies made on these interesting neoplasms appeared in direct support of previous investigations by Fischel (10) who contended that granulosa cells and theca cells were derivatives of the ovarian mesenchyme. All the histological varieties of granulosa-cell tumor were produced, including luteinized examples which, on account of their slow evolution, were interpreted as possibly representing a ripening stage of the more "immature" folliculoid and trabecular forms (Traut, Kuder, and Cadden, 42). In most of the experimentally produced neoplasms an admixture of granulosa and theca cells occurred and this the authors interpreted as denoting an origin from a common stem. However, the occurrence of practically pure forms of both types was a strong argument against those who doubted the existence, in human beings, of pure theca-cell neoplasms (Thomson and Stabler, 41; Novak, 28, 29). Undoubtedly many corollary problems will be solved as further studies are carried out on these roentgen-produced neoplasms.

That the pituitary gland may play a part in the histogenesis of granulosa-cell tumors was suggested by the recent work of Biskind and Biskind (2). Starting with the premise that the liver destroys estrogen, they set up a series of biological experiments in which they castrated female rats and implanted portions of the removed gonads into the spleen. The portal circulation picked up and destroyed any elaborated estrogen, preventing it from reaching the general circulation and

[1] Inasmuch as many of the histogenetic, clinical, and pathological data are common to both varieties of feminizing ovarian tumors, they will be discussed, for the most part, under the present heading for the sake of brevity.

consequently allowing the gonadotropic hormones of the pituitary body to act "unopposed." Whether or not this reasoning was correct, the fact remains that the implanted ovaries, in several instances, became the seat of typical granulosa-cell tumors. Further studies along this line of approach may yield interesting data.

On the clinical side, the age incidence of granulosa-cell tumors had undergone changes in interpretation. It was formerly believed that the majority of granulosa-cell tumors occurred beyond the time of the menopause. It now appears that the symptom, amenorrhea, so often ascribed to "the menopause" was merely the first symptom of a granulosa-cell tumor. Revising our figures accordingly we find that perhaps more than 50 per cent of the neoplasms arise during the period of sexual activity. From 5 to 10 per cent occur before the age of puberty and the tumor in question still stands as the prime cause for sexual and somatic precocity (Lull, 24). The remainder of the tumors apparently arise after the climacteric. Amenorrhea, as suggested previously, is being recognized more and more as occurring frequently (often early) in the life cycle of granulosa-cell tumors, and most investigators are agreed that it reflects a high level of circulating estrogen. The bleeding which so frequently follows or interrupts these periods of amenorrhea is believed to be a "withdrawal phenomenon" consequent on degeneration, necrosis, or hemorrhage in the tumor (Henderson, 20; Fuller and Smith, 11). It has also been postulated as resulting from a lowering of tumor estrogen associated with luteinization of the tumor cells (Traut, Kuder, and Cadden, 42). Good support of the hypothesis of "withdrawal" is afforded by cases in which the uterus is preserved at operation for removal of the ovarian tumor (4). Under these circumstances "amenorrheic" patients almost invariably "menstruate" within forty-eight hours of the time of operation. Among postmenopausal patients suffering from this type of neoplasm, uterine bleeding still appears to be the most important symptom. However, while the bleeding occurs with a certain amount of rhythmicity, it rarely assumes the regularity of menstruation (as was formerly suggested, 7). However, the "discontinuity" of the bleeding and the fact that it is always more than a mere "spotting" remain as salient features in the differential diagnosis of granulosa-cell tumor from uterine carcinoma.

Laboratory studies carried out on the blood and urine of patients, while disappointingly few (Bland and Goldstein, 3; Palmer, 30; Schuschania, 36; Thomson and Stabler, 41), support strongly the evidence afforded by pathological studies that estrogen is elaborated in large amounts. The amount of circulating hormone drops precipitously following operative removal of the tumor (Fuller and Smith, 11). Bio-assays carried out on tumor tissue have yielded variable results (13). A frequent finding of none or only small quantities (Voigt, 45) of estrogen in such tissue suggests that the substance is not long retained at its source or is intermittently secreted. Biological activity has been proved in connection with experimentally produced granulosa-cell tumors. The existence of progesterone within luteinized examples, although strongly suggested in the endometrial studies cited later (Giordano and Haymond, 15; Karsner, 22), has as yet not been clearly demonstrated in the experimental laboratory.

Gross surgical pathological findings have remained much the same as those described in the earlier cases. For the most part the tumors are solid, well encapsulated, and rarely of extremely large size. Ascites—sometimes hemorrhagic—has been noted and a concomitant hydrothorax occasionally appears as with fibromas in Meigs' syndrome (Vogt, 44). Rupture of the tumor capsule, especially in adherent examples, should warn the operator against the danger of recurrence. Voight (45), Powell and Black (31), and Ragins and Frankel (32) recently reported granulosa-cell tumors of extraovarian (retroperitoneal) origin.

Microscopically, no new types[1] have been added to those described prior to 1939, but special stains have been employed recently to bring out cellular details heretofore not shown by routine methods. Greenhill and Greenblatt (17), Traut and Marchetti (43), Dockerty (6), and others have pointed out the frequency with which "theca-granulosa-cell" tumors occur. Traut and Marchetti (43) and Henderson (20), moreover, found that granulosa cells are reticulum-free whereas theca cells are often surrounded by this substance. Foot and Gomorri stains have been employed as differential diagnostic agents but with variable success. Similarly, distinctions based on stains purporting to reveal qualitative and quantitative differences in lipoid content of granulosa-cell and theca-cell tumors (Greenblatt, Greenhill, and Brown, 16) are difficult of interpretation (Karsner, 22). Stabler and Thomson (39) showed that whereas there were clinical differences in the lipoid content of functioning as

[1]The occurrence of cartilage in an otherwise typical granulosa-cell tumor was first described in 1933 by Schiller (34), who termed the tumor a desmoblastoma. Solomons and Dockeray (38) reported a similar finding. However, many believe, like Karsner (22), that these neoplasms are probably atypical teratomas.

opposed to nonfunctioning ovarian tumors, there were no outstanding differences among members of the former group.

At the present time the tendency is to reject the thesis that the human corpus luteum is ever the seat of neoplastic transformation. Accordingly, now included under the subtitle of "luteinized granulosa-cell tumors" are certain neoplasms which were formerly termed luteomas. From a purely histological point of view it may at times be difficult to distinguish differences between these neoplasms and those arising from renal and adrenal rests (hypernephromas and masculinovoblastomas). At times evidence from the clinical history of the case and the results of hormone determinations may prove invaluable aids in the matter of classifying the tumor. The necessity of carefully weighing such evidence is well afforded by the case of Giordano and Haymond (15), wherein a granulosa-cell tumor developed in a patient who had been "masculinized" from an early age. Metastatic ovarian neoplasms (renal carcinoma) may pose the same problems. As a matter of fact, at times the trabecular and diffuse types of arrhenoblastoma may closely mimic granulosa-cell tumor in microscopic structure.

The degree of malignancy in granulosa-cell tumors, histologically, is still a matter for future studies to decide since to date no definite criteria have been established to clarify this most important issue (Ingraham, Black, and Rutledge, 21). Clinical recurrences or metastasis, or both are said to occur all the way from 4.5 per cent to 33 per cent in different series. Reported "recurrences," on the one hand, fail to take into account the possibility of the development of a second primary granulosa-cell tumor in the contralateral ovary and, on the other hand, the possibility that the author included in his series examples of anaplastic small-cell carcinomas of the ovary (Seegar and Jones, 37). Moreover, the finding of late recurrences and metastasis (Dockerty and MacCarty, 8; McCartney, 25; Harris, 19) makes one chary of accepting, as final, statistics based on short-term survivals following surgical removal of this type of neoplasm. From the practical standpoint it can be remembered that the well encapsulated granulosa-cell tumor rarely recurs, that the adherent or ruptured neoplasm is more likely to do so, and that recurrence and metastasis are nearly always confined to the older age groups wherein the need for conserving the uterus and the contralateral ovary is not of paramount importance.

Associated pathological lesions have received their share of attention. These include a myohypertrophy observed by most investigators (Dockerty and MacCarty, 7). In the case of Russell (33) the wall of the uterus measured 2½ inches (6 cm.) in thickness. Fibromyomas have been reported as involving the myometrium in more than 50 per cent of the cases. Adenomyoma (McCartney, 25) has been recorded. The first two findings are consistent with the effect of estrogen stimulation (Lipschuetz and associates, 23; Marx, Glass, and Shulman, 26). With the endometrium, the presence of "cystic glandular hyperplasia" is being constantly recorded and studied in the light of an estrogen effect. Recently, luteinized granulosa-cell tumors have been observed, with a concomitant picture of secretory endometrium (Giordano and Haymond, 15; Novak, 29) and occasionally decidual change (Karsner, 22). This suggests that these ovarian hormones may in fact elaborate progesterone in addition to estrogen. The presence of intrauterine pregnancy is very rare in association with granulosa-cell tumor but can occur with small neoplasms (Henderson, 20; Schulze, 35). However, pregnancy has followed the removal of granulosa-cell tumors in young women (Powell and Black, 31; Harris, 19; and in my series, 6). Carcinomas and carcinomalike hyperplasias of the endometrium and endocervix (Stohr, 40; Russell, 33; Henderson, 20; Novak, 29) have been reported in an incidence exceeding that afforded by pure chance. The lesions are known to occur in the experimental animal as a result of estrogenic stimulation (Allen, Danforth, and Doisy, 1). The occasional association of mammary enlargement, fibroadenomas (McCartney, 25) or even mammary carcinoma (Fuller and Smith, 11; Allen, Danforth, and Doisy, 1; Finkler, 9) may have a similar significance.

The treatment of granulosa-cell tumors has been established along definite lines which in general dictate conservatism for young women and a tendency toward more radical procedures among older patients. In the latter group the dangers of endometrial carcinoma and of recurrence and metastasis of the ovarian tumor are deciding factors. The benefits of roentgen therapy employed postoperatively have not been evaluated on large series and, in any case, probably will always remain doubtful in tumors with such a low rate of clinical "malignancy." There is some evidence (Dockerty and MacCarty, 8) that granulosa-cell tumors may be radiosensitive. Advantage may be taken of this observation in cases in which complete operative removal is an impossible or doubtful accomplishment.

Before leaving the subject it may be well to remind the readers that precocious puberty may be

caused by ovarian cysts (Mengert, 27) associated with conditions like Albright's syndrome (Davis, 5; Stabler and Thomson, 39), and possibly related to the presence of certain tumors of the brain and of the adrenal gland (Gross, 18). In other instances (Lena Medina of Peru) no tumor may be present to which to attribute the phenomenon.

THECA-CELL TUMOR

Theca-cell tumor, the "newest" member of the group of functioning ovarian neoplasms, has the misfortune of behaving physiologically like a granulosa-cell tumor and demonstrating pathologically many of the features of granulosa-cell tumor and of ovarian fibroma. Consequently we find men like Meyer denying the existence of all but a few examples and classifying the remainder as fibromas with fatty metamorphosis. Novak (9), on the other extreme, while accepting the "functioning" examples, points, in these, to the almost variable presence of granulosa cells as the "incretory" elements, and proposes an all-inclusive term, "feminizing mesenchymoma," to cover both groups. The majority of investigators (1) including Geist and Spielman (5) follow along with Loeffler and Priesel (8) in giving the neoplasm a place in the family of ovarian tumors and a "credit rating" of almost 100 cases. Like their granulosa-cell "relatives," theca-cell tumors can be produced experimentally in mice through the use of roentgen rays. Their origin, in common with granulosa-cell tumors, may be traced to the ovarian mesenchyme. In the experimentally produced tumors, it must be admitted, mixtures of granulosa and theca cells are commonly encountered in the same neoplasm. However, as suggested previously, pure types of both lesions are found. With such an origin, therefore, it is not surprising that in the human subject granulosa cells are discovered in many examples of theca-cell tumor and vice versa.

From the clinical standpoint, although both of the aforementioned tumors produce almost identical symptoms, theca-cell tumor is found at a much later age period than is granulosa-cell tumor (Patterson and McCullagh, 10). Whereas the latter is seen before the age of adolescence in from 5 to 10 per cent of the cases, the former is very rarely observed among patients who are less than thirty-five years of age. Clinical symptoms common to the other member of the "feminizing" group of tumors are present in the thecomas, although not as constantly. In approximately 25 per cent of cases there are no symptoms suggestive of endocrine dysfunction. This is adduced by some as evidence that the group has been "diluted" by the addition of "fatty fibromas." To others it merely signifies that theca cells are ordinarily not so prodigious in their capacity to produce estrogen as are granulosa cells.

From surgical and gross pathological angles theca-cell tumors are almost always unilateral and benign, but several cases of malignant theca-cell tumors have been recorded in the literature; namely, those of Loeffler and Priesel (8) and of Geist and Gaines (4). The tumors are usually solid, encapsulated (Perlmutter, 11) and frequently yellowish and firm on section. Ascites is occasionally encountered and in at least 1 instance (Perlmutter) a concomitant existence of hydrothorax completed the features of Meigs' syndrome. The histological highlights have been repeatedly emphasized with recent attention paid to the frequent admixture of granulosa cells. Novak (9) claims that their presence is necessary before symptoms of "hyperestrinism" are produced. Special studies have shown that granulosa cells contain argentaffin granules which are lacking in theca cells and this point has been utilized in differentiating granulosa-cell tumors from theca-cell tumors. The employment of stains for reticulum fibrils and of special stains for lipoids, as well as the chemical procedures (fractional lipoid determinations) designed to separate incretory from nonincretory tumor groups have been previously outlined. As mentioned in a foregoing paragraph, evidence is not conclusive that these tests can be depended on when ordinary histological methods pose certain problems of differential diagnosis. On the other hand, most workers will agree with Greenblatt, Greenhill, and Brown (6) that a high phospholipid determination may denote that a given tumor is a theca-cell neoplasm rather than an ovarian fibroma which has undergone fatty degeneration.

Evidence is forthcoming that theca-cell tumors are estrogenic (Geist and Spielman, 5; Voight, 13) and consequently we are not surprised when we read reports of concomitant uterine myohypertrophy (Dockerty, 2), fibromyomas (Wolfe and Neigus, 14; Fallas, 3), adenomyomas (Wolfe and Neigus) and carcinoma of the uterine fundus (Wolfe and Neigus, Porter and Bramhall, 12; Kirshbaum, 7) and of the uterine cervix (Perlmutter, 11). It is the feeling of many that the high incidence of these associated lesions cannot be explained on the basis of pure coincidence. The treatment of theca-cell tumor follows the general principles outlined for granulosa-cell neoplasms. The necessity for preserving the uterus and the contralateral ovary is not often pressing because of the ages of the patients. The possibility of uter-

ine carcinoma should be constantly kept in mind. On the other hand there is little likelihood of recurrence of, or metastasis from, the theca-cell tumor.

ARRHENOBLASTOMA

More than 75 of these neoplasms have not been recorded in the medical literature and with each new accumulation the problem of histogenesis seems to increase in complexity. Ten years ago most investigators were quite ready to accept as final Meyer's hypothesis of origin (19), in which the tumor was said to be derived from overgrowth of male-directed elements within the hilus of the ovary. However, although in birds (Friedgood and Uotila, 7; Allen, 1) an apparent reversal of sex accompanied tumors of this type, it was apparent that in human beings, the more "testicular looking" the neoplasm, the fewer the masculinizing symptoms (Krock and Wolfermann, 12). Moreover, as noted by McCartney (14) and by Bell (3), the androgenic effects of the tumor could not always be correlated with the presence or absence of interstitial (Leydig) cells. In spite of these unexplained facts most investigators support Meyer's hypothesis. Popoff (24) in 1930 and McLester (16) in 1936 were among the first to suggest the thesis that arrhenoblastomas are, in essence, teratomas with an overgrowth of androgenic (testicular) elements. In the tumors which they studied tissues were found microscopically which could not possibly have been testicular in nature. In 1940 Kanter and Klawans (9) provided another case in support of the hypothesis of "teratomatous" origin. Krock and Wolfermann (12) in 1941 observed cartilage in a recurrent nodule of tumor and reviewed the whole subject of heterologous tissues which had been found in association with arrhenoblastoma. Surprisingly enough they discovered a 34 per cent incidence of elements which included bone and cartilage, thyroid tissue, mucinous and ciliated epithelium, fat, and so forth, alone or combined.

An origin of the tumors by way of thwarted overgrowth of "ovotesticular gonads" in pseudohermaphrodites obtains support from a few isolated cases in the literature. In this category one might include Novak's cases of "testicular tubular adenoma" occurring in 2 sisters (22). Some confusion (or perhaps disguised light) has been added to the problem of histogenesis by the cases of Meyer (18), of Plate (23), and of Mechler and Black (17) in which there existed within the same tumor the paradoxical combination of granulosa-cell and arrhenoblastoma elements. To these "hybrids" the term "gynandroblastoma" has been applied. In reporting their case Mechler and Black reviewed a group of 21 cases in which a diagnosis of masculinizing granulosa-cell tumor had been entertained. Many of the latter appear to have been examples of granulosa-cell tumor in which amenorrhea had been interpreted as being a masculinizing symptom. This we now know to be by no means true. Additional examples seem to have been instances in which granulosa-cell tumors affected women who were of masculine habitus and whose masculinizing aspects were in no way influenced by the development of, nor by the removal of, the neoplasm. There remained, however, a residue wherein the ovarian tumors seem to have produced masculinizing characteristics along with the "feminizing" features of uterine hypertrophy and menometrorrhagia. The origin of these latter neoplasms is as difficult to interpret as are their complex hormonal manifestations.

On the clinical side the age "limit" of patients with arrhenoblastoma has been extended recently by the unusual case reported by Kny (11). His patient with *bilateral* arrhenoblastomas was sixty-six years old. The presence of ascites was the unusual clinical sign in the case reported by Kanter and Ragins (10). Symptoms of masculinization have varied tremendously in degree and have not always correlated with "expectations" based on microscopic studies as previously suggested. The matter of differential clinical diagnosis has recently been stressed by Dorfman, Wilson, and Peters (6) who pointed out that the presence of striae, hypertension, diabetic tendencies, plethora, "buffalo-humping," and loss of libido, along with the roentgenological finding of osteoporosis, are features not usually associated with the masculinization of arrhenoblastoma. All of these features, embodied in the Cushing syndrome, suggest a neoplasm of adrenocortical origin. As stated elsewhere in this article, the ovarian "masculinovoblastoma" of Rottino and McGrath (25) typically gives rise to this syndrome. Sterility as a symptom has received attention in reports by Lisser, Palmer, and Morton (13), MacCarty and me (5), Althabe, di Paolo, and Colillas (2), of instances wherein pregnancy has followed removal of an arrhenoblastoma.

Always regarded as being more or less malignant clinically, this feature has received recent emphasis by Novak (21), by Kny (11), and by Krock and Wolfermann (12). These last-named investigators observed recurrence and death from metastasis ten years after removal of the primary growth. In 1 of the cases reported by MacCarty and me in 1939 (5) the patient, after a symptom-free interval, again became masculinized. This

patient has recently succumbed to the results of metastasis twelve years after her operation.

In the matter of laboratory diagnosis, Kanter and Klawans (9) record the new finding in arrhenoblastoma of a low level of blood sodium and a high value for blood potassium. Urinary-excretion values for both of these substances were unusually low. Results of hormonal studies carried out on the blood and urine of patients with these tumors have not been very enlightening. Recently Kanter and Klawans, and Boltuch (4) noted slight increases in the urinary output of androgenic substances. Perhaps future studies based on urinary determinations for certain 17-ketosteroid fractions may prove to be helpful.

Grossly the tumors have generally been solid throughout and of small to moderate size. As noted by Geist (8), however, certain cystic examples may become very large. A fairly constant finding has been the presence, on cut section, of a degree of lobulation not commonly observed with ovarian tumors of other types. Microscopically, the classification of Meyer (18), who divided arrhenoblastomas into tubular, trabecular or intermediate, and diffuse or sarcomatoid patterns, still remains good teaching. Interstitial or Leydiglike cells may be difficult to find and Kanter and Ragins (10) recently advised the employment of fluorescent microscopy as a means of facilitating their demonstration. The presence of these interstitial cells bears only a general relationship to the clinical picture of masculinization. As suggested in the foregoing paragraphs careful microscopic search should be carried out for elements which are nontesticular (of teratomatous origin). Finally, it must not be forgotten that at times the diagnosis cannot rest solely with the microscopist (Norris, 20; McIntyre, 15). Occasionally even the combined clinical and pathological picture taxes the diagnostic wits of a trained "endocriminologist."

Treatment of these tumors, occurring, as they usually do, in the early years of sexual activity, consists of local surgical removal of those which are encapsulated, and periodic examination for symptoms and signs of early or late recurrence. For adherent and infiltrating examples of this type and for arrhenoblastomas affecting women who have passed the menopause, total removal of the pelvic sexual organs is not too radical.

ADRENAL-LIKE OVARIAN TUMOR ASSOCIATED WITH CUSHING'S SYNDROME (SO-CALLED MASCULINOVOBLASTOMA, LUTEOMA, HYPERNEPHROMA, ADRENOCORTICAL CARCINOMA OF THE OVARY)

In 1944 Kepler, Priestley, and I (9) collected the available literature listed under the foregoing headings and presented data on a personal case—the fourteenth instance of the condition. The following is a summary of our findings, amplified by more recent contributions by Greene and Lapp (5), Mayer (10), and others.

Of the four hypotheses of histogenesis, that which derives these tumors from the corpus luteum seems to be the most unlikely. This structure is very evanescent and its physiological functions are such that one would expect clinically from any tumor engendered therein, the exact opposite of Cushing's syndrome (Schiller, 13). Almost as much "against the nature of things" is the hypothesis that some of the neoplasms arise through luteinization of granulosa-cell tumors. Yet in the case of Giordano and Haymond (4), clinical masculinization was present in the face of an endometrium which reflected an effect of progesterone (lutein hormone). Equally puzzling was the case of Stewart (14), in which there was a high excretion of urinary pregnandiol associated with the presence of a masculinizing ovarian hypernephroid tumor. In view of this evidence it might be well before discarding this second hypothesis to consider the possibility that the hormones produced by luteinized granulosa-cell tumors may not be the same as those elaborated by normal luteinized granulosa cells (Rottino and McGrath, 12).

To many the hypothesis that these adrenal-like ovarian neoplasms (Schiller) arise from adrenocortical ovarian rests seems to be the most plausible. The apparent rarity (Novak, 11) of these rests in the ovaries of adults is explained by Grollman (7) on the grounds that they are present at birth but disappear later. He relates the disappearance of these elements to the concomitant regression of androgenic tissue within the adrenal gland itself and the persistence and hyperplasia to clinical virilism. That such a thesis is worthy of consideration is attested by some experiments of Groat (6) in which young ground squirrels were subjected to bilateral adrenalectomy and maintained on an adequate diet supplemented with an augmented intake of chlorides. Histologically, the ovaries of the animals which survived showed a pronounced proliferation of cells resembling those of the adrenal cortex. Whether these proliferations represented growth of adrenal rests or, as Groat suggested, metaplasia from the ovarian mesenchyme seems immaterial in view of the important fact that the ovaries in these animals became "adrenal-like" in appearance and in function.

Geist and Gaines (3) report an almost identical change occurring within the ovaries of suckling

rats following the administration of gonadotropins. The condition was associated with degrees of masculinization in the animals. These authors also recorded 2 cases of clinical masculinization in patients who demonstrated, without actual formation of tumor, ovarian changes similar to those described by Groat. Ovarian resection was not accompanied by clinical improvement. However, in a comparable case recorded recently by Fraenkel (2) and termed "hyperthecosis" of the ovary, masculinization disappeared and pregnancy followed the removal of one ovary and resection of the second. Turner (15) in 1943 reported a somewhat similar result in his case. The fourth hypothesis of origin, namely, derivation through teratomatous channels, is possible but has not been proved.

Clinically, as with adrenocortical carcinomas, the ovarian tumors under discussion produce the symptoms and signs which characterize Cushing's syndrome. To the masculinization which accompanies the arrhenoblastoma must be added, in a typical case, hypertension (6 cases), polycythemia (4 cases), and a tendency to diabetes (5 cases). Plethoric obesity and osteoporosis are additional features which relate the tumors functionally to primary neoplasms of the adrenal cortex. Evidences afforded by hormonal studies on the urine of patients suffering from the effects of these neoplasms have given some conflicting results. Various investigators have noted increases of estrogen and androgens and even the excretion of pregnandiol. At the present time urinary estimations of certain 17-ketosteroid fractions seem to hold some promise in the matter of differential diagnosis but more work needs to be done along this line of investigation (Kepler, Dockerty, and Priestley, 9).

Grossly all but 1 of the 15 reported adrenal-like ovarian tumors have been unilateral with no particular predilection for either side (Rottino and McGrath, 12). The more malignant examples may be adherent and associated with local or distant metastatic nodules (Barzilai, 1), but for the most part the neoplasms are encapsulated. Their size is generally small to moderate. A yellow color on cut section is usually noted but variations in color from hemorrhage and necrosis are also common.

The microscopic picture is essentially that of epithelial-like polygonal cells arranged in trabecular or pseudoalveolar pattern recalling the architecture of the adrenal cortex. Grouping in cell aggregates separated by coarse or fine strands of connective tissue and an intimate relation to the sinusoidal and capillary blood spaces heighten the similarity. Further resemblance to the cells of the adrenal cortex is afforded by a high cytoplasmic content of fat and of glycogen. Moreover, special stains (Ponceau-fuchsin) serve to identify certain granulations which, although not confined to, are quite characteristic of, adrenocortical cells of the androgenic zone. Yet withal it must be admitted that from a purely histological standpoint it may be impossible to distinguish between the tumor in question and luteinized granulosa-cell tumor or metastatic hypernephroma (Kannerstein, Brown, and Rosen, 8). The eventual diagnosis may at times rest on evaluation of the combined clinical, hormonal, chemical, and pathological aspects of the case. Similarly, from a histological standpoint the malignant potentialities are difficult of evaluation. Tumors which were cytologically malignant have not recurred. Death from metastasis has been observed in 1 instance only (Rottino and McGrath, 12). With this in mind and with the knowledge that the majority of tumors arise during the period of reproductivity, conservative surgical treatment should be employed for most of the tumors of this type. When age is not a factor and in instances wherein local extension of the neoplastic process has occurred, more radical measures are indicated. The importance of postoperative therapy with adrenocortical preparations cannot be overemphasized inasmuch as signs of adrenal insufficiency are otherwise prone to develop (Kepler, Dockerty, and Priestley, 9).

DYSGERMINOMA OVARII

Within the past ten years this neoplasm has been removed from the group of round-cell sarcomas and, correctly, we believe, has been given an individual membership in the family of ovarian tumors. Although the designation "seminoma ovarii" is still occasionally appended, for the most part the term "dysgerminoma" has largely replaced the older terms such as embryonal carcinoma, germinal cell blastoma, large round-cell sarcoma, and so forth. Although a considerable volume of knowledge has accumulated as a result of the 200 odd cases reported in the literature, there are many features of dysgerminoma which still remain obscure.

Meyer (14, 15), who first proposed this histogenetically suggestive appellation, did so in support of his concept of origin from "neutral" or "dysgerminal" cells similar to those found in both male and female gonads before the actual stage of sexual differentiation. His hypothesis is additionally supported by the following facts: (1) the tumor occurs in both sexes (seminoma testis is identical with dysgerminoma ovarii in all major pathological details); (2) the neoplasm is the com-

monest tumor of the gonads of pseudohermaphrodites; (3) it has a relatively high incidence in maldeveloped and misplaced gonads, especially in undescended testes; and (4) females suffering from the condition, if not actually hermaphroditic, frequently demonstrate lack of development of their sexual organs (infantile condition of the uterus and so forth). Although Ewing (5) felt that dysgerminoma represented an atypical teratoblastoma, gynecologists have not too strongly emphasized this histogenetic possibility and practically all are at present content with the Meyer hypothesis.

Clinically the tumors, which were formerly stressed as occurring nearly always during the first two decades of life, have recently been reported as affecting women in the third, fourth, and fifth decades (Kirshbaum and Newman, 12; Dockerty and MacCarty, 4; Geist, 9). Moreover, whereas the tendency formerly was and currently is for emphasis on the "neutral" and occasionally masculinizing effect on the host (Hohage, 11), a number of cases are now coming to light in which pregnancy has preceded development of the tumor (Dockerty and MacCarty, 4; Kirshbaum and Newman, 12) or has actually been a complication of dysgerminoma (Lorber and Vesell, 13; Dockerty and MacCarty, 4; Cunningham and McGrath, 3; Stabler and Thomson, 19). In several instances conservative surgical procedures in the treatment have made possible the successful development of a subsequent pregnancy. Feeney (6) recently reported the only instance of dysgerminoma which occurred in an achondroplastic dwarf.

Studies on hormone production have been inadequately prosecuted and one gathers the impression that any evidence of hormonal imbalance may not be directly attributable to the tumor so much as to the "sexually imbalanced status" on which the dysgerminoma is superimposed. On the other hand, gonadotropic hormones are sometimes present in excess in the urine of men with seminoma testis (Ferris, 7). Moreover these hormones, in the absence of tumor metastasis, disappear from the urine following orchectomy. Similar findings for dysgerminoma have recently been recorded by Hohage (11) and by Spielman and Morton (18) (tumor extracts). In 1 of our cases of dysgerminoma the patient had a strongly positive Ascheim-Zondek reaction, which became negative following removal of the neoplasm and the application of roentgen therapy over the metastatic deposits. In the case of Lorber and Vesell (13) the urinary output of estrogen was within normal limits.

The clinical degree of malignancy of these tumors has only recently received its deserved emphasis. Föderl's estimate of a 68 per cent recurrence rate (8) supports the contention of Kirshbaum and Newman (12) that dysgerminoma is very malignant. Observed at laparotomy, dysgerminoma is a large, semisolid tumor which, although usually encapsulated, may be fungating and accompanied by bloody ascites. Bilateral involvement is present in almost a third of the cases and the smaller tumor may be mistakenly looked on as an enlarged but otherwise normal ovary. Subsequent growth on the contralateral ovary may therefore masquerade as an "inoperable recurrence" of a tumor which had been removed previously. Intraperitoneal metastasis may be observed at the time of operation. Occasionally the primary site may be other than ovarian (Schiller, 17).

The microscopic characteristics of dysgerminoma are too well known to merit another detailed account. The epithelial cellular anaplasia with scattered nests of lymphocytes and occasional epithelioid cells and giant cells occurs in a monotony which is duplicated only by the identically composed seminoma testis. The giant cells have recently been restudied by Heller (10), who decided that they, like the lymphocytes and the epithelioid elements, represent a chronic inflammatory reaction to the presence of lipoid deposits derived from degenerating and necrotic tumor cells. Sailer (16) remarked on the occasional finding of granulosa-like cells in certain dysgerminomas.

The treatment for the neoplasm follows the same general lines laid down for arrhenoblastoma. However, the tendency toward conservatism is tempered by the knowledge that the patients are often sterile because of an underlying pseudohermaphroditic condition, that the tumors are frequently bilateral, and that they are all highly malignant microscopically. The surgeon who leans too heavily on the statistics of "pregnancy following local removal of dysgerminoma" does so at the risk of inviting metastasis. The effects of roentgen therapy have not been overstudied in tumors of this type but the observations of Cabot and Berkson (1, 2) indicate that the similar tumor of the testis is extremely sensitive to the effects of roentgen rays.

BRENNER TUMOR

Although the Brenner tumor has been known to gynecologists for almost forty years, over half of the 200 odd cases recorded to date have been studied within the past decade. The histogenetic

hypothesis of Meyer (8), who derived the neoplasm from Walthard rests, is accepted by the majority including Novak (10), Danforth (3), and Varangot (17), although it is still unproved. The main obstacle to the general acceptance of the hypothesis arises from the frequency of Walthard-cell rests underneath the serosa of the fallopian tube and the absence of Brenner tumors arising from this location. Schiller's hypothesis of origin from wolffian remnants (14) still faces the obstinate fact that anatomic connection between muellerian and wolffian systems (within the ovarian confines at least) has not been satisfactorily proved as yet. Barzilai (2) accepts Schiller's concept so far as to designate the epithelial elements in these tumors as paramalpighian cells. Sutton and McDonald (16), on the other hand, have described tumors of the subtrigonal glands which, although arising from the selfsame cells which Schiller "used" in his hypothesis, resembled ovarian tumors of the Brenner type in no pronounced degree. Teratomatous origin has been postulated because of the association of Brenner tumor and mucinous cystadenoma, a tumor which is itself regarded by many as being a teratoma wherein mucous glands have crowded out the other elements (Dockerty and MacCarty, 4). Novak (10) and Meyer (8), however, reverse the interpretation by stating that the mucinous portions of these cysts developed from the Brenner tumor elements. For the time being, however, everybody seems happy to use the designation "Brenner tumor" proposed by Meyer in deference to the man who first described the neoplasm accurately.

Although a few Brenner tumors have been associated with postmenopausal bleeding clinically (Marwil and Beaver, 7; Novak, Dockerty, and MacCarty, and others), there is no direct evidence that the neoplasm supplies the necessary hormone or hormones to account for this system. Moreover, as Novak has pointed out, postmenopausal hypertrophy of the endometrium occurs in the absence of ovarian neoplasms. Rogers (13) found pregnancy complicated by Brenner tumor in 5 cases, including the 1 he reported. Ascites has been recorded as a clinical manifestation, and recently, in the tumor reported by Kelemen (6), hydrothorax completed the picture of Meigs' syndrome. It appears that there are no clinical symptoms or signs which are pathognomonic of a Brenner tumor. Similarly, a gross surgical diagnosis is rarely possible.

Pathologically we find a substantial incidence of bilateral involvement (13 in the literature) as a result of careful examination of the contralateral ovary (Fox, 5; Peale, 11). The tumors on an average are smaller than fibromas, but Neiman (9) and Reel and Foster (12) have reported very large neoplasms. While the majority are described as being solid throughout, resembling fibromas, the incidence of the type associated with mucinous cysts still stands at about 33 per cent. Microscopically the tumor has maintained its consistently "benign record" and no undoubted examples of malignant Brenner tumor have been reported. Simpson and Branch (15), however, point out the difficulties of distinguishing atypical Brenner tumors from primary ovarian adenoacanthomas of a low order of malignancy. The only cytological studies made recently in connection with tumors of the Brenner type have been those of Danforth (3), of Varangot (17), and of Arey (1), who attempted to compare the "grooving" observed within the nuclei of the squamous epithelial elements with similar phenomena observed in Walthard-cell rests, Sertoli cells, fibroblasts, and smooth muscle. The results of these studies are as interesting as their practical applications are obscure.

MESONEPHROMA OF THE OVARY

In 1939 Schiller (9) described a group of 10 ovarian and parovarian neoplasms which, although possessing no specific gross characteristics, microscopically appeared to constitute a new oncologic entity of possibly mesonephric derivation. The tumors were partially or completely solid, frequently large, and occasionally papillarylike ordinary cystadenocarcinomas. Microscopically the essential composition was that of "parvilocular" cysts lined by cells which seemed to be halfway between endothelial and epithelial. They were characterized by long bases, a shallow "depth," and the presence of projecting, or "hobnail," nuclei. Cytoplasm was abundant and well stained. Even more distinctive was the presence within the cysts of papillary projections showing centrally loose connective-tissue cores, poor in capillaries, and, peripherally, a covering mantle of cells continuous with and similar to those lining the cyst cavities. In the latter situation transition to cells of a more definitely epithelial character was observed but the cells of the papillary mantle nearly always maintained their endothelial appearance. The stroma surrounding these glomeruluslike units was infiltrated by similar endothelial-like cells which were frequently atypical and anaplastic. Here also collagenous tissues helped provide a framework for the "glomeruli" and for the occasionally encountered tubule-like structure which was also possessed of this same peculiar endothe-

lial-like lining. Edema of the stroma was frequently observed. Schiller believed that the presence of these glomeruluslike structures signified an origin of the tumor via mesonephric rests and attempted to show by serial sections and wax-model reconstruction a strong resemblance between the afore-mentioned units and primitive mesonephric glomeruli with their capillary-poor tufts and their scant supply of connecting tubules.

In a later communication made in 1942, Schiller (10) described a renal neoplasm of comparable type which, he felt, supported his histogenetic concept. Another neoplasm which arose from the right broad ligament he interpreted similarly. An observed predilection of these tumors for right ovarian involvement he correlated with the known facts regarding maldevelopment and "rest-richness" of the right ovary in certain lower forms, notably in birds. His contentions favoring a pure mesonephric origin for these neoplasms were somewhat weakened by his inclusion within the group of small tumors which were undoubtedly examples of malignant teratoma. Moreover, the actual existence of mesonephric ovarian rests has never been actually demonstrated.

In 1940 Jones and Seegar (4) reported 6 cases of ovarian mesonephroma. They believed that the microscopic patterns described by Schiller were perhaps sufficiently distinctive to warrant separation of the tumor from the general group of ovarian carcinomas, but they did not feel that the resemblance of the intracystic papillary tufts to mesonephric glomerulii was striking enough to decide the important matter of histogenesis. Five of their 6 tumors were on the right side. Perforation of the tumor capsule was related to clinical recurrence and metastasis. In a subsequent article, based on a study of 17 cases, Jones and Jones (3) emphasized the seriousness of the condition with 10 of 15 traced patients failing to survive operation for more than two and one-half years. In 1 case only did they observe a marked beneficial response to roentgen therapy.

In recording data on 3 tumors of this type Kazancigil, Laqueur, and Ladewig (6) in 1940 expressed the belief that the tumors were endothelial and not epithelial, and proposed the name "papilloendothelioma ovarii" as being more correct than that of mesonephroma. They repeated the wax-model reconstruction attempts of Schiller but were unable to confirm the latter's interpretation of the glomeruluslike structures. On the other hand, they found what they interpreted as representing islands of hematopoietic tissue within one of their tumors and utilized this finding to support their "endothelial" hypothesis. The demonstration of mucus in one of their tumors and the association of dysgerminomalike regions in another raised again the possibility of their fundamentally teratomatous nature. All 3 tumors were considered as being malignant. The right ovary was involved in 2 instances. Tuta and Siebel (12) in 1941 and Rosenblatt and Grayzel (8) in 1942 reported single examples of mesonephroma and agreed in principle with Schiller's concept of the histogenesis. Stromme and Traut (11) in 1943 added 10 examples, of which (for a change) 8 were in the left ovary. They could not visualize how tumors with such express degrees of dedifferentiation could possibly produce innocent glomerular structures, but, on the contrary, they felt that a teratomatous origin was the correct histogenetic interpretation. Upon reading their article one cannot escape the feeling that these authors included neoplasms which more properly belonged in other categories. In 1943 Jensik and Falls (2) reported 1 of the few cases with bilateral ovarian involvement. With controversy highlighting interpretations of the existence as well as the nature of this new entity, we find Barzilai (1) accepting and Novak (7) disagreeing heartily with the glomerular notion of histogenesis. Karsner (5) felt that neoplasms containing mucus-secreting cells should be excluded from the group. Faced with these issues and observing that so-called mesonephromas present no distinctive symptoms, receive no different treatment, and offer no different prognosis, as compared with well known anaplastic forms of ovarian carcinoma, most gynecologists appear to be withholding their judgment along with their case reports, until time has clarified the afore-mentioned problems.

SECONDARY TUMORS OF THE OVARY INCLUDING KRUKENBERG'S TUMOR

Of all the pelvic viscera, the ovary seems to be the most favored site for involvement in metastatic malignant processes. Two main primary sources furnish us with the majority of these secondary ovarian tumors, namely, (1) carcinoma arising within the pelvis (uterine fundus, fallopian tube, pelvic colon), and (2) carcinoma arising within the upper part of the gastrointestinal tract, the gallbladder, and the pancreas. To the latter must be added the occasional case of mammary carcinoma, melanoepithelioma, and so forth. The first general group entails few difficulties of interpretation, inasmuch as the ovarian involvement is often by direct contact or by very obvious lymphatic extension (Lynch and Dockerty, 8). Moreover, the secondary ovarian deposits duplicate the primary growth in microscopic appearance.

Reports concerning the second group revolve chiefly around what for the past forty years has been termed the Krukenberg tumor (5). This neoplasm was originally described as demonstrating frequent bilateral ovarian involvement by large, solid, lobulated tumors preserving in general the contour of the normal ovary. The microscopic structure was highly distinctive and consisted of an essential fibromyxomatous composition with a scattering of signet-ring cells. Krukenberg thought the tumor to be primary in the ovary, and a sarcoma. Later Schlagenhaufer (13) and others showed that these characteristics were duplicated by certain matastatic ovarian cancers, notably of gastric origin, and the signet-ring elements were the key to a corrected diagnosis of carcinoma rather than sarcoma. Jarcho (4), Major (9), Masson (10), Copland and Colvin (2), to name a few, advanced strong evidence in support of the metastatic concept and Ewing (3) went so far as to state that primary ovarian tumors of the Krukenberg type did not, in fact, exist. Most investigators, however, felt that certain examples like those of Andrews (1) and of Schiller and Kozoll (12) were exceptions to this general rule and that certain malignant mucinous ovarian cystadenocarcinomas could very closely mimic the picture of metastatic carcinoma of the Krukenberg type.

Three prime issues provide fuel for current controversy in connection with these peculiar neoplasms: (1) What constitutes a Krukenberg tumor? (2) By what means do these tumors arrive at their ovarian destination? (3) What is the proper treatment for these tumors? On the first of these matters there are two schools of thought. Certain men (Schiller and Kozoll, 12; Novak and Gray, 11) feel that one should confine the material to neoplasms which show in major part the picture of signet-ring cells without any glandular formation in a fibromyxomatous stroma. In essence, accordingly, they would be limiting the cases almost exclusively to metastasis from anaplastic mucus-producing scirrhous carcinoma of the stomach, for mammary, colonic, and pancreatic carcinomas are infrequently of this type. Almost invariably, however, we find the supporters of this thesis slipping into their case reports, photomicrographs of "atypical" fields in which good glandular acini are depicted and in which no mucus is present. Others, including Leffel, Masson, and Dockerty (6), point out the futility of confining the group to a small handful of high-grade (Broders) carcinomas of mucous type when neoplasms of a lower order of malignancy produce identical gross ovarian involvement and an almost identical fibroblastic reaction in the ovary. According to the interpretations of these different investigators the number of "acceptable" cases ranges from 153 (Copland and Colvin, 2) to more than 300 (Lubin and Polayes, 7).

In the pathogenesis of ovarian involvement the hypotheses of peritoneal sedimentation, lymphatic permeation, and blood vascular spread all have their proponents. In favor of the peritoneal sedimentation hypothesis we have the observations that endometrial cells, mucous cells (ruptured mucinous cysts), and splenic cellular elements can "implant" and proliferate on peritoneal surfaces. We know, moreover, that carcinoma cells are present and multiply in ascitic fluid of malignant derivation. Moreover, in the absence of true lymphatics within the central nervous system, metastasis from gliomas obtains by a process of true sedimentation in the cerebrospinal fluid. The "freshening" of the ovarian surfaces by the periodic rupture of follicles may or may not explain the relatively high incidence of Krukenberg tumors among women of childbearing age. Cases (Leffel, Masson, and Dockerty, 6) with early and exclusively cortical involvement would appear to be best explained by this hypothesis.

The presence in certain cases of Krukenberg tumor of peritoneal carcinomatosis and the high incidence of bilateral ovarian involvement are taken by others (Masson, 10; Copland and Colvin, Lubin and Polayes, 7) as an indication that the carcinoma cells reach the ovaries via the peritoneal lymphatics. Other cases have been observed in which extensive involvement of the periaortic and pelvic lymph nodes suggested lymphatic extension to the ovaries by the retrograde method (Jarcho, 4). The number of complete autopsies on cases of this type has not been sufficient to demonstrate in all cases the "blockage" of higher chains of nodes which is necessary before retrograde extension can occur.

The evidence of blood vascular spread, while available in a few cases (Major, 9), does not appear to obtain in others. From the standpoint of practicability it appears that, whatever the mode or modes of dissemination to the ovary, this organ by no means is the only site for the metastatic deposits, as evidenced by an eventual mortality rate very closely approaching 10 per cent.

Clinically, as pointed out by numerous investigators, symptoms referable to the primary neoplasm are overshadowed by those of the ovarian lesions in about 35 per cent. Abdominal ascites is present in a third of the cases. The cardinal point for the surgeon is to keep in mind the possibility that bilateral, solid, lobulated, ovarian tumors

may, in fact, be metastatic, and to investigate conditions within the upper portion of the abdomen, particularly the condition of the stomach. The problem of curing a metastatic carcinoma is different from that of eradicating a primary growth. Moreover, removal of, let us say, a gastric primary neoplasm along with its ovarian secondaries, does not, as indicated, accomplish "complete eradication" of the carcinomatous process. Perhaps local removal of the ovarian tumors with a forestalling of complications consequent on twisting of the tumor pedicles accomplishes as much eventually, as the more heroic measures cited previously. Exceptions to this dictum will, of course, obtain in the group wherein the primary malignant process is uterine or colonic. In these patients cure can sometimes be effected by radical surgical operations followed by therapy with roentgen rays.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

EYE

Schall, L. A., and Reagan, D. J.: Malignant Exophthalmos. *Ann. Otol. Rhinol.*, 1945, 54: 37.

The authors discuss surgical decompression of the orbit to relieve symptoms and preserve vision in primary and in post-thyroidectomy malignant exophthalmos.

In classic Graves' disease, increased activity of the thyroid produces the clinical picture of hyperthyroidism. An excessive amount of thyrotropic hormone of the anterior pituitary gland is also produced, but it is in turn inhibited by the excessive thyroxin which its stimulation of the thyroid has produced.

In the orbit there is a generalized edema and lymphocytic infiltration of the orbital contents, particularly of the extraocular muscles.

Loss of vision (in malignant exophthalmos usually following thyroidectomy) attributed to pressure and tension at the optic nerve, papilledema, and peripapillary hemorrhages are usually associated with diplopia due to limitation of rotation of the eyeball, especially upward. Advanced cases are associated with edema of the eyelids and conjunctiva, and the presence of firm retrobulbar resistance to pressure by the fingers. In still more advanced cases, the eyelids cannot be closed, and keratitis, ulceration, and even endophthalmitis may result.

The following features differentiate the classic from the ophthalmopathic types of exophthalmic goiter:

	Classic	Ophthalmopathic
Sex incidence	Females 9:1	Females 50; males 50
Hyperthyroid symptoms	Moderate or marked	Little or none; patient may be hypothyroid.
Exophthalmos	Average 2.5 mm.	Average 7 mm.
Basal metabolic rate	High	Normal, slightly elevated, or low.
Effect of iodine and thyroidectomy	Usually marked improvement	Useless; may aggravate condition.

Some cases can be controlled by thyroid extract or x-rays directed to the orbits; others require surgical decompression of the orbit. In Naffziger's technique two frontal bone flaps are made to expose the orbital roofs, which are removed as far back as the optic foramen. The anterior rim of the orbit is preserved to maintain the contour of the brow. The accessory nasal sinuses are not entered.

Sewall, in 1936, suggested utilizing the space provided by the nasal sinuses for orbital decompression. He suggested removal of the ethmoid sinus, the floor of the frontal sinus, and in some cases the medial floor of the orbit. Kistner, in 1938, treated 2 patients satisfactorily in this way. According to Kistner, and the authors who performed the operation in 2 cases, the chief advantages of the method proposed by Sewall and first used by Kistner, are as follows:

This procedure is not only less disfiguring than the Naffziger operation, but it utilizes an actual rather than a potential space. Moreover, in some cases the roof of the orbit is occupied by an extension of air cells, which the Naffziger technique avoids, and subjective and objective pulsation (which may follow the intracranial operation) does not occur in this procedure.

JOSHUA ZUCKERMAN, M.D.

Crawford, R. A. D.: Repair of Perforating Corneal Wounds. *Lancet*, Lond., 1945, 248: 366.

A series of 34 cases in which repair of perforating corneal wounds was accomplished by corneal sutures is compared to a group in which conjunctival flaps were used. No minor perforations were included, and all cases studied were without a retained foreign body.

Those cases in which a traumatic cataract developed showed less satisfactory end-results. Sulfathiazole was used but no penicillin. The comparative study with the flap procedure showed little difference in the end-results.

The important factors involved are the technical difficulties associated with the placing of the sutures as balanced by the more rapid healing, restoration of the anterior chamber, and the elimination of infection.

HUNTER H. ROMAINE, M.D.

Carson, L. D.: Ocular Effects of Altitude Flying and of Deep Sea Diving. *Arch. Ophth.*, Chic., 1945, 33: 173.

Changes in atmospheric pressure in flying are within the range between the pressure at sea level (1 atmosphere) and that at the maximum altitudes now attainable by military craft (1/6 atmosphere). Pressure encountered in deep sea diving can also be expressed in terms of pressure at sea level, ranging from 1 to 6, 7, or 8 atmospheres.

The ocular effects of changes in atmospheric pressure may occur as part of a general anoxic syndrome, as accidents resulting from localized obstruction, or from phenomena due to direct pressure which affects the nutrition of the retina or the innervation of the intrinsic or extrinsic ocular muscles. Inasmuch as military flying at altitudes above 10,000 feet requires the use of oxygen, severe degrees of anoxia are usually encountered only in cases of failure of the supply of oxygen or leakage of masks at great altitudes.

Symptoms of anoxia, which may persist from one to sixty hours, vary with the altitude and the duration of flight. These include: partial blindness, right homonymous hemianopsia, binasal blurring, nystagmus, spots before the eyes, scintillating scotomas, diplopia, yellow vision, and ocular pain.

With respect to the effects of glare, the author recommends that the ideal goggles for flying should be so designed as to fit snugly into the oxygen mask, should contain no optical defect in the unshatterable material and should be so ventilated as to be free of fogging in order to provide an unrestricted field.

In the discussion, Conrad Berens referred to the preliminary work on anoxia carried out in World War I. HUNTER H. ROMAINE, M.D.

EAR

Shambaugh, G. E.: A Comparison of the Improvement in Hearing following the Fenestration Operation with that Obtained by Wearing a Hearing Aid. *Arch. Otolar.*, Chic., 1945, 41: 189.

With a new type of audiometer which measures the hearing for speech rather than for pure tones, it has been found that patients who experience an average or greater than average hearing gain from the fenestration operation have as good or better hearing for speech than they formerly had from their hearing aid. Patients experiencing a less than average improvement in hearing (a gain less than 20 decibels) do not hear as well as they did with a hearing aid.

On the basis of the one-year results obtained through application of the fenestration technique, the prospective ideal subject for the fenestration operation may be told that he has approximately a 90 per cent chance of a lasting improvement in his hearing and approximately a 70 per cent chance that his hearing will equal or surpass that which he has with a hearing aid. NOAH D. FABRICANT, M.D.

NOSE AND SINUSES

Hauser, I. J., and Work, W. P.: The Treatment of Sinusitis with Penicillin. *Arch. Otolar.*, Chic., 1945, 41: 161.

Penicillin is a most important adjunct to other forms of treatment for sinus disease and the complications of this disease. The authors' method of choice for administration has been to inject intramuscularly 20,000 units every three hours until the optimum results have been obtained. In the treatment of orbital cellulitis this proved to be so dramatically effective that in their practice it has replaced every other method of treatment. While in cases of allergic rhinitis with superimposed infection this treatment eliminated all evidence of suppuration, the authors did not believe that it effected a permanent cure inasmuch as the underlying pathological state, allergy, was still present. Patients with chronic suppurative sinusitis of relatively short duration can apparently be cured by penicillin alone. In long-standing chronic suppurative sinus disease, however, penicillin alone appeared to have little if any value; used in conjunction with adequate surgical treatment it accomplished rapid and complete cures. NOAH D. FABRICANT, M.D.

MOUTH

Beiswanger, R. H., and Stenstrom, K. W.: Carcinoma of the Cheek, Alveolar Processes, Floor of the Mouth, and Palate. *Radiology*, 1945, 44: 213.

The authors review 160 cases of carcinoma of the alveolar processes, the cheek, the floor of the mouth, and the palate, which were treated during the years from 1926 to 1940, inclusive, in the Section of Radiation Therapy of the University of Minnesota Hospitals, Minneapolis. In 129 cases the diagnosis was confirmed by biopsy.

Clinically, the lesions were grouped into 4 stages: (1) under 1.5 cm. in diameter, 2 cases (1 per cent); (2) over 1.5 cm. in diameter with no local extension, 34 cases (21 per cent); (3) with local extension, 54 cases (34 per cent); and (4) with metastases on admission, 70 cases (43 per cent).

The ages of the patients ranged from thirty-six to eighty-eight years, the average age being sixty-five years, so that cancer of the oral cavity must be considered predominantly as a disease of old age.

The most common etiological factors were strong tobacco (26 per cent), leucoplakia (27 per cent), ill-fitting dentures (6 to 8 per cent), syphilis (5 per cent), and dental sepsis (95 per cent).

The percentages of metastases amounted to 40 for the upper alveolus, 35 for the lower alveolus, 55 for the cheek, 43 for the floor of the mouth, 30 for the hard palate, and 73 for the soft palate.

The treatment comprised 3 phases: (1) hygienic care of the oral cavity; (2) treatment of the primary lesion; and (3) management of the cervical metastases.

The hygienic measures consisted of removal of the bad teeth, mouth washes, irrigations, vitamin therapy, and discouragement of the use of tobacco.

The treatment of the primary lesion was by a combination of surgery and radiation therapy, or by radiation therapy alone. Radon was used extensively in almost all of the cases.

During the various periods certain technical changes were made. At the present time the preferred method is the application of radium molds to the primary lesion, and external irradiation with roentgen rays over a period of from twenty-one to twenty-eight days. Gold radon implants are then inserted into soft-tissue lesions and around the metastatic nodes. If any persistence is noticed two months later, a radical dissection is done in operable cases. The roentgen irradiation is carried out with 220 kv., 1 mm. of copper, multiple fields being used for crossfiring; approximately 3,000 roentgens of roentgen rays and from 4,000 to 7,000 roentgens of gamma rays are delivered to the lesion.

No prophylactic neck dissection was performed to avoid cervical metastases. However, as soon as such metastases became manifest they were treated with external irradiation, radon implantation, and block dissection. Far advanced cases were given palliative radiation therapy only.

The final results are tabularly compiled for each of the groups. A 24 per cent five-year survival rate was obtained for all cases. In addition, in 61 per cent of stage 2 lesions, and 60 per cent of stage 3 lesions palliation was obtained for from one to five years.

It is expected that with further progress in the technique of roentgen irradiation, such as direct intraoral therapy or the application of higher voltages, these results may be improved within certain limits. T. LEUCUTIA, M.D.

NECK

Jackson, A. S.: The Use of Thiouracil in Hyperthyroidism; 10 Illustrative Cases. *Am. J. Surg.*, 1945, 67: 467.

The author has had experience with 30 cases of hyperthyroidism treated with thiouracil. Because of the danger of intoxication, he uses the drug with caution. He states that among 2,000 cases in this country which were treated with thiouracil, there were 7 deaths from agranulocytosis.

The author is doubtful whether thiouracil is a safer drug than iodine for the preparation of a patient for operation. He used the former in the following 6 types of hyperthyroid patients: (1) advanced cases of multiple toxic adenoma not responding to iodine; (2) cases of toxic adenoma complicated by myocarditis, fibrillation, hypertension, decompensation, and diabetes; (3) cases of exophthalmic goiter in which, because of pregnancy, previous nerve injury, infections, or other diseases, it may be desirable to delay surgery without iodine therapy; (4) cases of iodine-fast exophthalmic goiter; and (5) cases of recurrent or persistent hyperthyroidism.

Cases treated with thiouracil exhibited an increased vascularity and tendency to bleed at operation, and the acini tended to be small and contracted, without colloid, and with an increase in the interstitial tissue. Postoperative reactions were minimal.

A patient with toxic adenoma, who would previously have required a two-stage operation, responded satisfactorily to a one-stage operation after preparation with thiouracil.

Ten detailed case records are given.

CLINTON H. THIENES, M.D.

Montague, J. R., and Wilson, C. P.: Thiouracil (Deracil). A Study of Its Use in 43 Cases of Thyrotoxicosis. *West. J. Surg.*, 1945, 53: 65.

The authors report 43 cases of thyrotoxicosis treated with thiouracil. The percentage of their successes and failures is essentially the same as in other series reported. They report only 1 toxic reaction, in which the patient had a temperature of 102° F., pulse 120, malaise and weakness, and a scarlatiniform rash. These symptoms disappeared three days after discontinuance of the drug. In no patient was there a depression of the granulocytes.

Early remissions were obtained in patients who had exhibited symptoms of thyrotoxicosis for relatively short periods.

Nineteen toxic nodular goiter cases were treated with improvement in 16 and no improvement in 3. Sixteen cases of toxic diffuse goiter were treated and all showed improvement. Eight patients discontinued treatment; in 1 the condition was improved, and in 3 it was unimproved; 4 patients were uncooperative. EARL O. LATIMER, M.D.

Gargill, S. L., and Lesses, M. F.: Toxic Reactions to Thiouracil. *J. Am. M. Ass.*, 1945, 127: 890.

The authors report the complications which developed in 8 of a series of 43 cases of toxic goiter treated with thiouracil since February, 1943. The dosage employed was from .1 to 1 gm. daily. The toxic reactions were as follows:

Agranulocytosis, 1 fatal case; jaundice, 2 cases; drug fever, 2 cases; and swelling of the submaxillary salivary glands, 2 cases. In addition, granulocytopenia occurred in a patient with severe heart failure who had been given the drug in an attempt to reduce myxedema.

In the fatal case of agranulocytosis, the patient had received 3 courses of thiouracil over a period of approximately one year. The first course lasted three months and the patient received an average daily dose of 0.2 gm. of thiouracil. This was followed by the development of myxedema, and a remission which lasted for a period of four and one-half months. The second course, in which the same daily dosage was used, was of fourteen weeks' duration. This was followed by a reappearance of myxedema and a remission of seven weeks. In the third and final course, the patient received the same daily dose of 0.2 gm. of thiouracil for a period of four weeks when agranulocytosis suddenly appeared. This patient died despite adequate treatment with penicillin, sulfadiazine, sulfamerazine, liver extract, and pentnucleotide.

The second patient on thiouracil developed a toxic granulocytopenia and dermatitis from which he recovered when the medication was stopped. His basal metabolic rate, however, remained unaltered, and two months later he died from recurrent heart failure. Autopsy revealed a normal thyroid gland and normal bone marrow.

The third patient did not respond to iodine medication and was given 0.8 gm. of thiouracil daily for ten days. After one week on this routine the patient developed dark urine and clay-colored stools. Following the removal of an apparently normal gall bladder the patient recovered, but the jaundice persisted for a period of over one hundred days.

The fourth patient had similar symptoms, but promptly recovered following omission of the drug.

The fifth and sixth patients ran temperatures which were undoubtedly secondary to the thiouracil medication.

The complications in the 2 remaining patients consisted of transient swelling of the submaxillary glands.

From this series of 43 patients, the authors conclude that although thiouracil is an effective drug

for the treatment of thyrotoxicosis, it may lead to serious uncontrollable, unpredictable toxic effects. Its use should be carefully controlled until satisfactory methods of preventing or controlling its toxic properties have been established.

SAMUEL J. FOGELSON, M.D.

Bjørneboe, M.: Re-Examination of 79 X-ray-Treated Exophthlamic Goiter Patients after from Eight to Eighteen Years following Their Discharge. *Acta med. scand.*, 1944, 117: 15.

In order to evaluate the efficacy of irradiation of exophthalmic goiter the author reviewed 115 patients treated for hyperthyroidism during the period from 1924 to 1934. The criteria of the diagnosis were the classical complaints: emaciation, sensation of heat, profuse perspiration, palpitation of the heart, nervousness, diarrhea, and the physical findings (nervous restlessness, tremor, tachycardia, enlargement of the thyroid gland, exophthalmos, warm, moist skin, and, from 1928, the metabolism rate). No distinction was made between exophthalmic goiter in the stricter sense of the word and toxic adenoma. Of these 115 patients, 22 were treated operatively. The remaining 93 were treated either with x-rays or drugs. In the autumn of 1942, i.e., from eight to eighteen years after the discharge of these patients from the hospital, the author tried to contact them. Information was obtained concerning 92: 17 have died, 69 were examined by the author personally, and 6 were examined by means of a questionnaire. Of the 92 patients, 7 were men and 85, women. Thirteen had been treated with stimulants, sedatives, and iodine, and 79 had been given x-ray treatment.

The 79 patients treated with x-rays included 38 with severe and 41 with mild conditions. Five had died, and 3 were suffering from affections other than goiter. Of the remaining 71 patients, 8 (11.2 per cent) were later treated operatively, while 7 (9.9 per cent) died; 44 (62.0 per cent) were well, and 12 (16.9 per cent) were ill; of the sick patients 3 suffered from cardiac insufficiency, 8 had a relapse of the hyperthyroidism, and 1 had myxedema.

As to the technique of irradiation, up to 1928 only one field—the anterior surface of the neck—was used, whereas since 1928 the x-rays are being applied from 3 directions—front, right, and left. The treatment was repeated at intervals of one or more months, according to the clinical symptoms and the rate of metabolism. The treatment was individualized with regard to the size of the single dose as well as to the frequency of the radiations. Thus, the duration of treatment varied from a single radiation or series of radiations to treatment through seven years. The only patient with severe changes in the skin had been treated previously in the earliest days of x-ray treatment.

The summary of the results shows that about two-thirds of the patients recovered under the treatment. The superiority of the operative treatment is frankly admitted by the author. The argument that x-ray treatment carries no mortality holds good only with certain reservations, because during the protracted treatment the patients are apt to die from thyrotoxic crisis or from their heart lesion which might have been cured by the operation. X-ray treatment has a limited field of usefulness, namely, in patients who either refuse the operation or suffer from a very severe hyperthyroidism. JOSEPH K. NARAT, M.D.

SURGERY OF THE NERVOUS SYSTEM

PERIPHERAL NERVES

Ehni, G., and Woltman, H. W.: Hemifacial Spasm. *Arch. Neur. Psychiat.*, Chic., 1945, 53: 205.

On the basis of 106 cases of hemifacial spasm occurring among 663 cases of pathological movements of the face of all sorts the following conclusions are drawn:

1. Women are more often afflicted than men, the ratio being about 6 to 4.
2. Children do not have hemifacial spasm.
3. Encephalitic illness or arteriosclerosis with or without hypertension seldom bears a causal relationship to hemifacial spasm.
4. The spasms usually begin in one orbicularis oculi muscle and slowly progress to adjacent muscles until, in certain cases, the entire facial musculature is involved.
5. Spontaneous remissions for periods up to three years have been noted.
6. The spasms in almost every case were aggravated by circumstances causing nervousness, fatigue, or voluntary movements of the face.
7. No patient was able to stop the spasms by an exercise of the will.
8. Only 5 patients were seemingly cured without resort to surgical treatment and 3 of these 5 may well be in periods of remissions.
9. Spinofacial anastomosis was performed in 3 cases with quite satisfactory results in all.
10. Argument is given for the view that the lesion causing this condition is in the facial nucleus or the proximal portion of the facial nerve.

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Hamby, W. B.: Gross Intracerebral Hematomas. *N. York State J. M.*, 1945, 45: 866.

This report is concerned with spontaneous, limited, removable intracerebral hematomas. Sixteen cases are reported in detail. Fourteen of the patients recovered following surgery, 1 died of massive postoperative pulmonary atelectasis, and 1 succumbed to a recurrent hemorrhage from a ruptured aneurysm of a major cerebral vessel.

Seven of the cases were associated with cerebral arterial disease (arteriosclerosis and/or hypertension and 1 bacterial endocarditis) and 5 with intracerebral neoplasm (3 metastases, 1 meningioma, and 1 astrocytoma). One case was proved (and 3 were suspected) to be due to ruptured aneurysms of the major blood vessels. One case was a delayed posttraumatic intracerebral hemorrhage.

The selecti n of cases for surgery from the common apoplexies still depends upon the criteria of Bagley: gradual progress of the clinical picture and development of signs of increased intracranial pressure after an acute onset of symptoms.

Those cases of intracerebral hematoma arising from aneurysms are most common near the rostral part of the circle of Willis, in the frontal lobes. They usually manifest themselves following a subarachnoid hemorrhage, the acute symptoms of which may clear. Signs then develop of an expanding cerebral lesion, and operation, following localization by ventriculography, discloses the hematoma, the walls of which are usually shaggy and stained with blood pigment. The aneurysm is usually not seen.

The cases associated with tumor may be followed by gratifying improvement, even though the tumor itself is not removable.

The lesion was located in the frontal lobe in 4 cases, the temporal lobe in 5, the occipital in 3, the cerebellar in 2, the parietal in 1 case, and in the ventricle in 1 case. Most other writers have reported these lesions as being found predominantly in the temporal or parietal region. However, there are many reports that all of the other areas, both infra- and supratentorial, are involved.

The age of the patients in this series ranged from thirteen to seventy-three years, the average being forty-one and eight-tenths years. Some writers have been impressed by the youth of the patients harboring these lesions.

The author was unable to reach any conclusion as to the type of clot to be found at any particular stage of these lesions. Old fluid blood can be obtained from almost all of them, and when the cyst is opened it always contains solid clot, at any time after the hemorrhage. Aspiration alone seldom empties any of these lesions. If the patient grows worse the lesion should be reaspirated or opened directly. Flushing out the cavity with colloidal thorium-dioxide suspension will make possible a later roentgenographic check upon the progress of the lesion.

Because of the formation of scar tissue in the walls of the cysts, epilepsy has developed both in operative cases and in those surviving without operation.

HENRY A. SHENKIN, M.D.

Dickerson, W. W.: Characteristic Roentgenographic Changes Associated with Tuberous Sclerosis. *Arch. Neur. Psychiat.*, Chic., 1945, 53: 199.

Two typical cases of tuberous sclerosis were completely examined to determine the location of the characteristic areas of calcification seen in the roentgenograms. Both patients were idiots with long histories of convulsive seizures, with sebaceous adenomas, cafe' au lait spots, and the characteristic areas of calcification in the skull. Autopsies were performed, and in each the usual findings of tuberous sclerosis were seen; many small white nodules were found in the surface of the brain with similar nodules situated subependymally in the cerebral ventricles.

Histological examination of these patches showed extensive gliosis.

Roentgenograms were then made of the specimens of the calvaria and the brains, and in each it was shown that the roentgenological peculiarities originated in the skull. X-ray examination of the fixed brain revealed nothing in either case. The areas of increased density in the skull when examined histologically showed hyperostosis of the inner table and of the trabeculae of the diploic spaces. The calvarium was also found to be of diminished thickness. Many of the islands of hyperostosis in the skull overlay tuberous nodules in the cerebral cortex.

ADRIEN VERBRUGGHEN, M.D.

Hofstatter, L., Smolik, E. A., and Busch, K.: Prefrontal Lobotomy in Treatment of Chronic Psychoses, with Special Reference to Section of the Orbital Areas Only. *Arch. Neur. Psychiat.*, Chic., 1945, 53: 125.

The authors decided to limit the operation of prefrontal lobotomy to section of the orbital region only, or of the lower quadrants of the frontal lobe. This was done with the hope that it would prove to be effective treatment and also restrict the extent of destruction and postoperative sequelae. A burr hole was placed 5 cm. above the zygomatic arch and 3 cm. posterior to the lateral rim of the orbit. The tip of the ventricle was located and a cut made in the coronal place to the depth of 5 cm. in front of the tip of the ventricle, from the level of the burr hole downward. This procedure was carried out bilaterally.

Twenty-two patients who previously had been judged as having a very poor prognosis were subjected to this modified procedure. All have been followed up for a period of twelve months or longer after operation. The condition was considered "much improved" when the patient could resume his social activities and return to his former level of occupation. It was considered as "improved" when the patient was able to make a better institutional adjustment, and "slightly improved" when he became a less troublesome nursing or custodial problem.

Three patients suffering from affective reaction types of psychosis, and who previously had had an average of 12 metrazol or electric shock treatments, were operated upon. Two of these, both agitated depressed individuals, were greatly benefited. The third patient, who had been in a chronic manic state, was benefited sufficiently to be returned to her family.

One patient with a obsessive-compulsive neurosis who had previously not responded to 7 metrazol or electric shock treatments, was greatly benefited.

Two neurasthenic patients, both of whom had been treated unsuccessfully with insulin and metrazol or electric shock, preoperatively, were greatly benefited by the operation.

Of 4 patients with epilepsy and psychosis, all of whom were operated upon, 1 was greatly benefited, and 3 were only slightly benefited by the procedure.

In the schizophrenic group, the condition was much improved in 7 cases, somewhat improved in 4, and slightly improved or not improved in 9. Hebephrenic patients showed the lowest rate of recovery, while the paranoid group showed the highest rate of response to operation.

No deaths, infections, or epileptic seizures have resulted from the procedure to date. Transitory incontinence developed in 4 of the 22 patients in whom only the lower quadrants were sectioned, as opposed to 4 of 8 patients in whom all 4 quadrants were sectioned. Two patients had mild, transitory hemiparesis, and in 2 others there was marked interference with speech, but this also was transitory. Postoperative confusion and disorientation were infrequently observed and had no effect on the outcome. Alertness and responsiveness on the first postoperative day did not affect the successful outcome of the operation. Improvement occurred within a few weeks, or after as long as a year.

In summary, a postoperative recovery rate of 40 per cent was obtained, a result comparing favorably with the average rate of recovery of 31.3 per cent of 17 other clinics. The incidence of transitory postoperative urinary incontinence was much lower, and postoperative dulling and slowing up were less pronounced with this modified operation. It was concluded that a satisfactory therapeutic result in patients with mental disorders was obtained with section of the orbital surfaces alone, and that the orbital areas of the frontal lobes have a role in regulation of the emotions. HENRY A. SHENKIN, M.D.

Cohn, R.: Electroencephalographic Study of Prefrontal Lobotomy; A Study of Focal Brain Injury. *Arch. Neur. Psychiat.*, Chic., 1945, 53: 283.

Cohn carried out electroencephalographic studies on patients before and after prefrontal lobotomy in order to determine the evidence of cerebral damage and how this evidence may help to interpret electroencephalograms in cases of accidental trauma.

The immediate abnormal electroencephalographic response to prefrontal lobotomy was focal (frontal) in conformity with the anatomic lesion. In all subjects from whom recordings were taken within ten days after operation high-voltage slow waves were observed in the symmetrical frontal leads. Within one to three months after operation, the prominent low-frequency waves (2 to 4 per second) were replaced by short sequences of 6 per second waves of reduced amplitude. In most subjects this low intensity abnormality persisted as a subdominant characteristic as long as recordings were made.

In 3 subjects, in whom the earliest recordings were made within one month after operation, no abnormal wave forms were recognized. Indeed, lobotomy induced the replacement of preoperative high-frequency waves by normal-appearing alpha waves. Reversion to the preoperative control record occurred nine months later.

Hyperventilation greatly accentuated the low-frequency characteristics of the electroencephalogram of lobotomized individuals which preoperatively were uninfluenced by a similar procedure.

It is evident from this work that old cerebral lesions give rise to focal and general electroencephalographic changes, and therefore the presence of prominent electroencephalographic abnormalities with old head injuries must be considered as being causally related to the cerebral damage.

On the other hand, this study also shows that even in the presence of known cerebral damage (acute or chronic), electroencephalographic abnormalities may be minimal or absent.

The effects of hyperventilation on the electroencephalogram after injury (lobotomy) demonstrates that neuronal disturbance is an important factor in the production of slow waves during the process of deep breathing. This clear finding makes it necessary to partially de-emphasize the role of alteration in the blood sugar in the production of slow waves during hyperventilation.

HENRY A. SHENKIN, M.D.

Meyer, A. H.: Meningococcal Meningitis; A Report on 165 Cases. *Ann. Int. M.*, 1945, 22: 543.

This series of cases of meningococcal meningitis was observed in the period from July, 1942 through May, 1944. One hundred and fifty cases were proved by direct smear or culture. The additional 15 cases were included because of the presence of a purulent spinal fluid and their occurrence in an epidemic period. The overall mortality rate was 5.3 per cent; for the proved 150 cases it was 4 per cent.

Six of the 9 deaths occurred in the first twenty-four hours of hospitalization. One death resulted from undue delay in diagnosis and only 2 deaths occurred after adequate treatment.

Therapy consisted of 5 gm. of sodium sulfadiazine given intravenously in a liter of physiological saline solution followed by 1 gm. given orally every four hours. A stomach tube was utilized for medication and the giving of fluids during coma. A fluid intake of at least 3 liters daily was maintained. Children were given an initial dose of sulfadiazine of 0.1 gm. per kgm. parenterally, followed by oral doses calculated on a basis of 0.2 gm. per kgm. The sulfadiazine blood level was maintained at 10 mgm. per 100 c.c. The sulfadiazine was usually discontinued on the ninth day of treatment. The only drug reactions were 9 instances of microscopic hematuria.

Meningococcus antitoxin was used in cases failing to respond to sulfadiazine within twenty-four hours, or when evidence of an overwhelming infection was noted on admission. Antitoxin was used in 39, or 23.6 per cent, of all cases. In patients under ten years of age the average dose of antitoxin was 20,000 units, the largest dose being 80,000 units. In patients over forty years old, the average dose used was 50,000 units, the largest being 120,000 units. The antitoxin was given in a single dose, half intravenously and half intramuscularly.

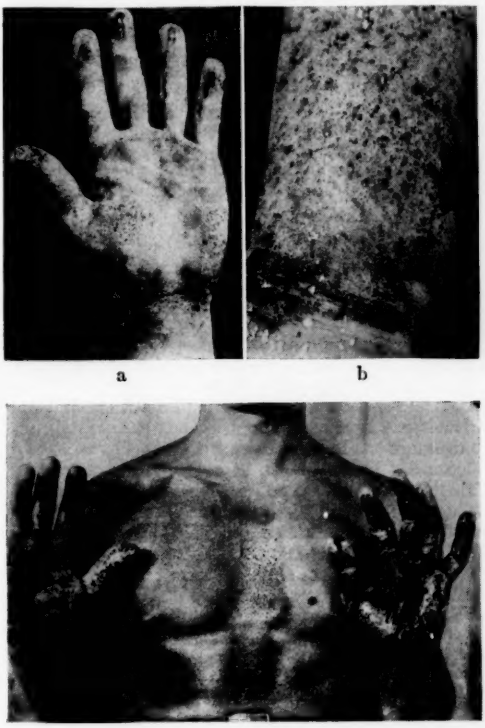
Repeated lumbar punctures were made to relieve increased intracranial pressure, as indicated by respiratory alterations and/or intractable headache or restlessness. The sequelae were: (1) relapse two weeks after discharge in a three-year-old child with subsequent recovery; (2) ulceration of a massive purpura in a patient with an overwhelming infection on admission, who recovered; (3) quadriplegia and respiratory paralysis, successfully treated by means of a respirator and lumbar puncture; (4) ptosis of one eyelid and unilateral optic atrophy; (5) 2 aseptic purulent effusions into knee joints and 1 aseptic purulent pleural effusion, all ending in recovery without drainage; (6) 2 instances of questionable hydrocephalus in infants; and (7) a hemiplegia in a fifty-nine-year-old hypertensive patient.

HENRY A. SHENKIN, M.D.

SYMPATHETIC NERVES

Silverman, J. J., and Powell, V. E.: A Simple Technique for Outlining the Sweat Pattern. *War Med.*, Chic., 1945, 7: 178.

A new technique for outlining sweat patterns is briefly described. The authors had previously de-



a b c

Fig. 1. A, Sweat pattern of the palm demonstrated with the technique of applying tannic acid directly to the skin; B, demonstration of individual sweat droplets over the forearm with the same technique. C, Another sweat pattern demonstrated by application of tannic acid.

scribed a method for showing the sweat pattern in the hand, and the new method is an adaptation of this one which is suitable for use over the rest of the body. The only chemicals used are alcohol, tannic acid, and ferric chloride. The ferric chloride is diluted with three parts of alcohol and applied to the skin with a cotton-tipped applicator. This evaporates rapidly and leaves a dry surface stained lightly with ferric chloride. An atomizer is then used to spray tannic-acid powder over the area. As the sweat glands function, the area sweating becomes diffusely blackened. ADRIEN VERBRUGGHEN, M.D.

MISCELLANEOUS

Lewey, F. H.: What Is the Guillain-Barré Syndrome? *J. Pediat.*, S. Louis, 1945, 26: 165.

The author points out the confusion which exists in the classification of certain polyneuritides, polyneuropathies, and ascending paralyses of radicular or spinal nature. The recent tendency has been to include all of these conditions under the so-called Guillain-Barré syndrome.

Two case histories representative of the Guillain-Barré syndrome are described, as well as the histopathological findings. Autopsy was done on a child who died unexpectedly in the fourth week of the disease from an acute degeneration of the phrenic nerves.

A comparison of the sacral nerve roots in these 2 cases was made possible by operative exposure of the sacral roots in the second case, which revealed swollen, adherent nerve roots from which sections were removed.

Pathologically, a peracute radiculopathy of almost necrotic nature was found. The myelin was pulverized and in many instances was found to be completely dissolved, while the axis cylinders were fragmented.

Further extensive involvement was demonstrated in the child at autopsy, as the phrenic nerves showed signs of acute irritation, evidence of cerebral arachnitis, cortical derangement, necrosis in the anterior horns, and degeneration in the white matter of the spinal cord; all of these conditions had failed to produce clinical signs.

The original conception of the Guillain-Barré syndrome was described as a severe but eventually benign polyneuropathy with preferential involvement of the motor nerves and albuminocytological dissociation in the spinal fluid.

It was pointed out, however, that in 1937 Guillain himself revoked this opinion without any reservations whatsoever.

The suggestion is made that the designation "Guillain-Barré syndrome" be retained as a general heading for the various forms of polyneuropathy and radiculopathy of unknown etiology, with or without encroachment upon the central nervous system, and a partial block as indicated by the albuminocytological dissociation in the spinal fluid.

HOWARD A. BROWN, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Buirge, R. E., Samuels, L. T., and McCartney, J. S.: The Treatment of Pubertal Bilateral Gynecomastia. *Surgery*, 1945, 17: 397.

The authors report a case of bilateral gynecomastia developing at puberty in a sixteen-year-old boy. It was associated with little beard development and some evidence of improper or subnormal testicular function. The 17-ketosteroid output was low. Administration of testosterone daily for three weeks decreased the volume of the breasts by about 50 per cent, while the general body weight increased. The excretion of 17-ketosteroids was also increased. The change in the gland appeared to be decreasing with time, however, and surgical removal was resorted to.

The histological picture was that of chronic fibrous mastitis. The case appears to have been another of the syndrome described by Kleinfelter, Reifenstein, and Albright.

While a considerable reduction in the size of the breasts can be produced in these cases by intensive treatment with testosterone, the result is not entirely satisfactory, probably because of the increased residual connective tissue. The surgical approach is to be preferred. Androgen therapy can be used subsequently if it seems indicated.

EARL O. LATIMER, M.D.

Biddle, A. G.: Improved Breast-Lifting Operation. *Am. J. Surg.*, 1945, 67: 488.

The author performs his breast-lifting operation under nerve-block anesthesia, and local infiltration about the nipple if necessary. The new location of the nipple is marked by means of a triangle which places the nipples 9 inches apart and in the third costal interspace. The first step in the operation is to cut a circle around the areola, with the nipple as a center. This is done by means of an electrical cutting point placed in a compass of the author's own design. A vertical incision is made from the lower border of the incisions down to the chest wall. The skin is next denuded from the entire surface of the breast, care being exercised not to puncture the skin and to follow the lines of cleavage. When the skin has been separated completely in all directions, three Lahey goiter clamps are used to hold the gland vertically. The fat is then removed from the breast; when the breast tissue is greatly oversized, a keystone-shaped section is excised from the upper central portion. Other sections are removed if necessary. The gland is sutured in its proper position and the skin fashioned around it and sutured.

The final step is to bring the nipple to the surface in its new location. The electrical cutting point and compass are again used. An opening slightly larger than the original areolar incision is made. The nipple is sutured in place with fine silk sutures. A pressure dressing is then applied.

EARL O. LATIMER, M.D.

Lamont, E. S.: Plastic Surgery in Reconstructing Enlarged Breasts. *Surgery*, 1945, 17: 379.

The author uses three types of procedure for mastopexy according to the individual case.

The one-stage mastopexy with transposition of the nipple may be used in the majority of patients with enlarged, hypertrophied breasts. The lines of incision are carefully measured and marked the day prior to operation. The initial incision is circular around the areola. From the center edge of this incision another is made perpendicularly upward to the new nipple site. The skin of the breast is undermined in a thick flap in the plane of cleavage. The breast entirely denuded of skin with its nipple and areola attached is pushed up to the desired position on the chest. Wedges of breast tissue are removed until the desired size is obtained. Following reconstruction of the breast three heavy silk sutures are taken through the pectoral fascia over the second rib, carried through the upper poles of the breast. Thus the breast is secured in its new position. A circular button of skin previously marked to serve as the new location of the areola and nipple is removed. The excess of skin is removed from the skin flaps and the skin edges are approximated. In reconstructing the opposite breast care is exercised to create symmetry and similarity between the two breasts.

In a markedly enlarged breast a two-stage operation with nipple transplantation may be the method of choice. In such cases the circular area which is to be the recipient bed for the nipple transplant is carefully measured and marked. An incision is made through part of the derma and the skin is dissected free to leave a bed for the reception of the nipple and its areola. An incision is made around the areola following a previously marked circle, and the structure is dissected free almost as a full-thickness graft. The nipple and areola are transplanted to the new site and a suitable pressure dressing is applied. Two weeks later the second stage is carried out. An incision is carried down from the center of the transplanted nipple; another incision is made along the under surface of the breast. Two thick skin flaps are created. The required amount of breast tissue is resected in the form of triangular wedges. The skin flaps are shaped and approximated in the form of an inverted T.

In excessively large breasts that have hypertrophied and retained an abundance of fatty tissue a two-stage mastopexy with transposition of the nipple is carried out. An incision is made around the areola, the desired amount of material being retained for transfer. From the center of the upper

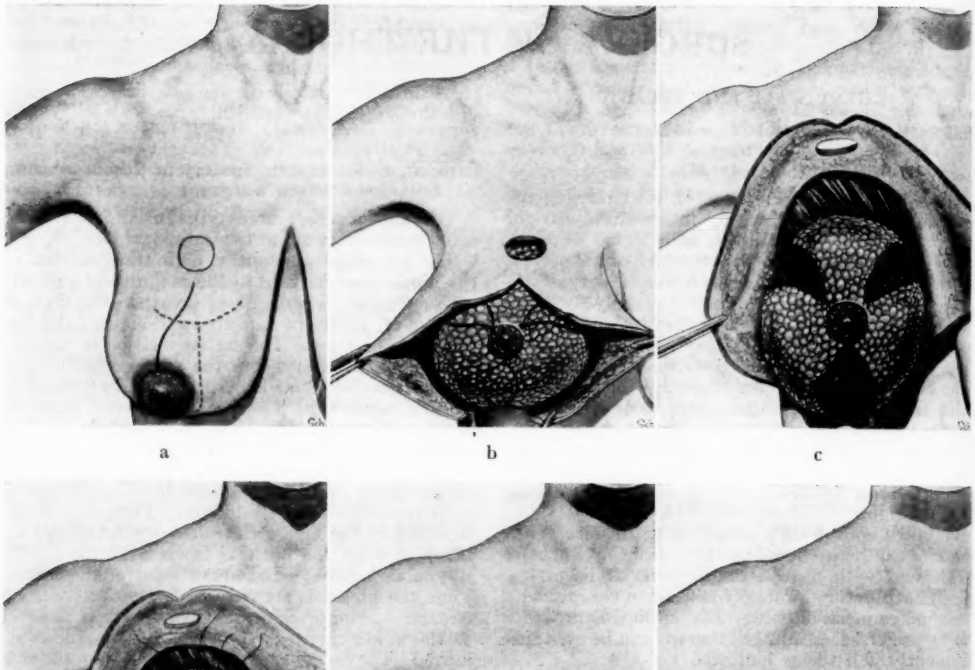


Fig. 1. Illustrations depicting author's modification of the one-stage mastopexy: *A*, The lines of incision have been carefully measured and marked, to indicate the new position of the nipple, the amount of areola to be transferred, and the size of the skin flaps. *B*, The skin is undermined in a thick flap. The nipple and its required amount of areola are left attached to the completely denuded breast. Triangular wedges of tissue are marked off to be resected with respect to the circulation. A circular button of skin is excised to create the new nipple site. *C*, The wedges of breast tissue are resected, and the required amount of material that will allow the reconstruction of a breast with the desired size, shape, and symmetry is removed. *D*, The breast tissue is united with silk and the upper pole is fixed to the pectoral fascia over the second rib with heavy silk sutures. *E*, The areola is sewn into its new residence. The skin flaps are so cut as to adjust themselves to the new size, contour, and position of the breast. *F*, The wound edges of the inverted T incision are sewn with interrupted silk sutures.

edge of this circle, an incision is carried perpendicularly upward to within a half-inch of the new nipple site. From the lower center of the circle an incision is carried perpendicularly downward to the inframammary line. Another incision about 10 cm. long is carried around the inframammary line to form an inverted T. One or two triangular wedges of breast are removed from the upper pole. The skin over the breast is undermined in a thick flap to an area just below the clavicle. The upper pole of the breast is fixed with three silk sutures to the pectoral fascia over the second rib. A circular area of skin is removed for the new nipple and areola site, and the nipple and areola are carefully sewn into place. The

excess of skin from the apron flaps is removed and the edges are sutured. A Penrose drain is inserted high into either corner of the wound. Two weeks later the previous line of incision along the inframammary line is opened and from its center edge an incision is made upward to the center edge of the areola to form an inverted T. Two thick triangular flaps are created to expose the medial and lateral poles of the breast. Two or three triangular wedges of breast are removed and, if necessary, a semicircular section is removed along the inframammary region. The required amount of skin is removed both from the center of each flap and from its inferior portion. A Penrose drain is placed in each angle of the wound. EARL O. LATIMER, M.D.

TRACHEA, LUNGS, AND PLEURA

Hayward, J. I.: The Removal of Blood from Traumatic Hemothoraces. *Austral. N. Zealand J. Surg.*, 1945, 14: 157.

The author discusses the management of cases of traumatic hemothorax in the New Guinea battlefront. There is still some controversy as to whether or not sterile hemothoraces should be aspirated. The author believes that the arguments against aspiration, such as the introduction of infection, the restarting of fresh hemorrhage, and the splinting effect of the blood on the lacerated lung, have been refuted.

Blood may clot in the pleural cavity in various ways and to different degrees, varying from short threads of fibrin to a large coagulum of fibrin. The fluid contents of different loculi may vary in color and consistency. The clotting varies from case to case and it is obvious that a number of factors are at play. The author believes that the factor of infection is an important one.

Blood may be removed from the pleural cavity by various methods such as, aspiration, intercostal tube drainage, and by rib resection and closed drainage. The cases in New Guinea were treated by repeated aspirations without air replacement. As a rule not more than 1 pint of blood was removed at a time and the process was repeated in three days. As these cases were treated up toward the front it was often necessary to subject them to aspiration on the way to the base hospital.

FORREST D. DODRILL, M.D.

Thomas, C. P., and Cleland, W. P.: Decortication in Clotted and Infected Hemothoraces. *Lancet*, Lond., 1945, 248: 327.

Hemothorax is by far the commonest complication in chest injuries, for it may be associated with any of the various types of injury produced by blast or crushing, in addition to penetrating and perforating wounds.

One must differentiate between a simple hemothorax which is the main or the most important effect of an injury, and the compound or complicated hemothorax in which the pleural blood is associated with a more serious or important injury to the lung, diaphragm, or chest wall. Almost all of the latter type of cases require active surgical treatment. The associated hemothorax, if removed at the time of operation, rarely causes further serious trouble. The simple hemothorax presents rather a different problem, for with adequate treatment it will usually resolve rapidly and completely. However, the mortality and morbidity in these cases depend almost entirely on the occurrence of infection or massive clotting in the hemothorax.

The extensive intrapleural use of penicillin has unfortunately been associated with a tendency to disregard the principles of early and frequent aspiration of blood from the pleural cavity, so that many cases remain virtually unaspirated for a considerable period.

Two fairly distinct types of clotted hemothorax have been encountered. One shows roentgenologically, multiple pockets containing air and fluid separated by strands, bands, or sheets of fibrin. The pockets are often shut off from each other and their contents may vary from sterile serous fluid to frank pus. The second variety encountered is the massive clot. In this type the clot is usually in one piece or a relatively small number of pieces, sometimes weighing as much as a pound.

The different appearances of these two types are due to the presence of air in the pleural cavity in the early stages. Such air may have come from the lung or through the wound, or it may have been introduced intentionally during air replacement. It is unlikely that gas produced by anaerobic organisms can wholly account for the differences as many multilocular cases are sterile, while infection of a massive clot with gas-forming organisms gives rise to a spongelike appearance roentgenologically. Gas-forming organisms undoubtedly accentuate the appearance of the multilocular variety.

The physical signs of the clotted hemothorax are essentially those of pleural fluid. In the multilocular cases areas of tympany and dullness may alternate. Breath sounds are usually absent, but sometimes they are present and then are bronchial in character. The occurrence of bronchial breath sounds depends on the state of the underlying lung; they are most usually heard when the lung is atelectatic.

The roentgenological features are sometimes distinctive but are commonly the same as in any pleural effusion. In the multilocular cases the appearance of multiple fluid levels is characteristic, but the condition may simulate the shadows thrown by the alimentary tract so that a diaphragmatic hernia may be suspected. Later cases with massive clotting show a sharply defined opacity as organization and contraction proceed, and small clots may assume an oval or spherical shape, resembling a chest-wall tumor or a peripheral growth of the lung.

The final diagnosis of clotting depends on the surgeon's inability to aspirate blood in reasonable quantities with an aspirating needle. Small quantities of blood can be aspirated even when a massive clot is present, because a little fluid blood is shut off in lo-

culi in the clot. Too often the aspiration of two or three ounces of fluid blood has led to the useless continuance of conservative treatment with unfortunate delay in the employment of more active measures. The inability to aspirate blood from a hemothorax does not always mean that clotting has occurred—the aspiration site may be too low because allowance has not been made for the usual rise in the diaphragm after injury; too small a needle may be employed; or the needle may be repeatedly blocked by small fibrinous tags floating in the fluid.

Much blood can unquestionably be absorbed from the pleural cavity, but even in minimal cases there is a certain amount of organization and fibrous-tissue formation. In the case of larger collections, considerable fibrous-tissue formation occurs; this may form a resistant corset, often an inch or more thick, around the lung and between it and the chest wall, to produce a condition suitably termed the "frozen chest." Organization with fibrous-tissue formation occurs with great rapidity in a hemothorax, and apparently takes place earlier and is more extensive in clotted cases.

Early and complete obliteration of the pleural space is the most important single factor in the prevention of pleural sepsis and its elimination when once established.

Earlier methods of treating clotted hemothoraces were attended by incomplete or considerably delayed lung expansion. At the best, such methods led to considerable deformity of the chest which in later life caused severe respiratory embarrassment. Less fortunate patients were left with severe and prolonged pleural infection, which was largely responsible for the mortality at the base hospital.

The employment of decortication with suction drainage fulfils the basic principle of early and complete re-expansion of the lung. The authors feel certain that the method will reduce markedly both the mortality and the morbidity of this group of cases.

An intercostal posterolateral approach through the sixth space, with resection of a segment of the sixth rib posteriorly, is employed for all but the small localized cases. In the latter group the incision is placed over the affected area. Good wide access is essential if the apical and diaphragmatic regions are to be reached easily. Blood and clot are first removed from the pleural cavity. The lung is then found encased in a red smooth membrane, with little or no respiratory excursion. This membrane is carefully incised until the gray shining layer of visceral pleura is encountered. A plane of cleavage is readily found between the pleura and the fibrous coat, and the latter is carefully removed from the lung by blunt dissection with the finger or a large curved hemostat, either closed or with a small swab in its jaws. Care must be taken to avoid lacerating the pleura, but a number of small tears seem unavoidable. It is inadvisable to try to remove the coating from the lung immediately adjacent to a lung wound, whether healed or unhealed, for to do so merely results in considerable pulmonary laceration. All lacerations of the pleura, either traumatic or operative, which still permit the leakage of air at the conclusion of the decortication should be sutured with fine catgut. If the diaphragm is covered with a fibrous-tissue coat, this coat should be removed and the costophrenic sinus reformed by breaking down the obliterating adhesions. The fibrous coating on the parietal pleura should then be removed as completely as possible. This is often a difficult task for purely mechanical reasons.

Intercostal drainage tubes are now inserted into the apical and basal regions of the pleural cavity. The apical tube is inserted through the highest available intercostal space between the vertebral border of the scapula and the vertebral column, while the basal tube (medium-bore, straight tube with a side hole) is inserted at the rib angles about 2 inches from the lower limit of the pleural cavity. The thoracotomy wound is then closed in layers.

During and after the operation, transfusion of whole blood is employed; from 2 to 3 pints of blood are usually necessary because shock may be severe, the patients are often poor operative risks, and hemorrhage may be significant, but is rarely excessive.

"Pentothal" with cyclopropane and oxygen given by the closed positive-pressure intratracheal method, has been used in most cases. When the fistulas have been large, nitrous oxide, oxygen, and ether have replaced the cyclopropane.

In the first place and for as long as demonstrable bronchopleural fistulas are present, both tubes are connected to water-sealed bottles. When the fistulas have closed—usually between twelve and thirty-six hours after operation—both tubes are connected by a Y-shaped connection to an electric suction pump. The pressure is reduced as rapidly as can be tolerated to 5 or 6 cm. Hg. In no case should suction be started until the patient is propped up on pillows after the operation. If suction is started when the patient is horizontal there is danger that the upper lobe may seal the upper catheter and leave an anterior pocket of air shut off from the tube. Suction is maintained for two or three days, and when the lung is fully expanded the tubes are removed; precautions should be taken to see that no air leaks along the tube tracks after removal of the tubes.

Hemothoraces occurred in 526 (70 per cent) of the cases in a series of 750 chest injuries. Infection was present in 30 per cent and clotting in 9 per cent of the hemothoraces. JOSEPH K. NARAT, M.D.

Fearnley, G. R.: Blast Injury to the Lungs. *Brit. M. J.*, 1945, 1: 474.

Experimental studies have revealed that the pathology due to explosive blast on the lungs is manifested by pulmonary hemorrhage of varying degrees of severity from small capillary surface bleeding to complete hepatization of the lungs. These lesions seem to be caused by the force of positive pressure directly on the chest wall.

The present report contained a clinical analysis of 21 such cases received at a base hospital from ten to

TABLE I.—SUMMARY OF CASES

Case	Explosive source; position	Time unconscious	Pain	Cough	Hemoptysis	Signs in chest	X-ray findings in chest
1	Aerial bomb; 50 yards Prone	0	21 days; retrosternal	21 days	1st–12th days; intermittent	Nil 2nd, 5th, 7th–21st days	Nil 2nd, 6th, 12th, 15th days
2	Mortar bomb; 3 feet Facing	8 hours	5 days retrosternal; 10 days upper abdomen	11 days; blood	1st–11th days; intermittent	General rhonchi 1st–3rd days	Nil 1st, 2nd, 3rd, 9th, 10th, 11th days
3	Aerial bomb; 30 yards Facing	0	5 days; retrosternal	8 days mucoid sputum	3rd–10th days; intermittent	Cyanosis, hyperexpansion and general rhonchi 1st day; nil 2nd day or later	Nil 2nd, 6th, 9th days
4	Land mine; 4 yards Left side	5 mins.	3 days; right chest	5 days; mucoid sputum	4th–9th days; daily	Nil 1st, 3rd, 5th, 9th days	Nil 4th, 7th days
5	Land mine; "close" Supine	0	6 days; retrosternal and back	5 days; bloody sputum	1st–5th days	Nil 1st, 2nd, 4th, 7th days	Nil 6th, 9th days
6	Mortar bomb; 5 yards Facing	5 hours	10 days; whole chest	5 days; blood	1st–5th days; daily	Generalized rhonchi 1st day; nil 3rd, 5th, 7th days	Nil 1st, 3rd, 8th days
7	Mortar bomb? ?	3 hours	7 days; whole chest, left arm	3 days; blood	1st–3rd days; daily	Generalized rhonchi 1st day; nil 3rd, 5th; 7th days	Nil 1st, 3rd, 5th days
8	Mortar bomb; 10 yards ?	5 hours	3 days; upper abdomen, left back	3 days; dry	3rd day	Nil 1st, 4th, 6th days	Nil 4th day
9	Grenade; 3 yards Right side	Few mins.	5 days; right chest	3 days; frothy sputum	1st day	Nil 4th, 6th days	Nil 4th day
10	Grenade; contact Left side	"Short time"	7 days; left chest and arm	7 days; mucoid sputum	1st–4th days	Generalized rhonchi 1st day	Nil 1st day; right interlobar fluid 3rd day
11	Mortar bomb? Right side	0	8 days; left chest	1 day; bloody sputum	1st day for 6 hours	Nil 1st, 4th days	Increased density left lower zone 4th day
12	Aerial bomb; 25 yards Prone	0	4 days; left chest	5 days; mucoid sputum	1st day	Cyanosis, rapid breathing, no signs in chest, 1st day; nil 4th, 6th, 8th days	Opacities both midzones 4th day; nil 8th day
13	Aerial bomb? Back to	Few mins.	2 days; retrosternal	1 day; blood	1st day	Generalized rhonchi 1st day; dullness and diminished B.S. at left base 5th day	Opacity left lower zone 5th day; opacity clearing 8th day
14	Aerial bomb? ?	? hours	2 days; right chest	1 day	1st day	Dullness and diminished B.S. at right base 1st day; diminished B.S. and creps. at right base 13th day	Heavy opacity right lower zone, small opacity left midzone, 3rd day; clearing on right, left side clear, on 6th day; nil 12th day
15	Flying bomb? ?	0	10 days; whole chest	Chronic bronchitic	0	Left hemothorax 3rd day; aspirated	Left hemothorax; clear by 24th day
16	Shell; 20 yards Back to	0	15 days; left chest	10 days; dry	1st day	Left hemothorax 2nd day; consolidation left base 12th day; clear 23rd day	Left hemothorax 2nd day; consolidation 13th day; pleural thickening 22nd day
17	Mortar bomb; close In trench	Few mins.	7 days; left chest	3 days; dry	0	Nil 3rd day; dullness left base 14th day	Nil 3rd day; opacity left base 14th day; almost clear 17th day
18	Flying bomb; 20 yards Back to	0	4 days; retrosternal and back	3 days; dry	0	Nil 1st and 2nd days; dullness, diminished B.S., and creps. right base 3rd day; nil 4th day	Nil 2nd and 4th days
19	Mortar bomb; 3 yards Left side	3 hours	14 days; retrosternal, left chest	0	0	Nil 1st day; dullness and diminished B.S. left base 3rd day; nil 8th day	Opacity left base 3rd day; cleared 8th day
20	Aerial bomb? Prone	6 hours	14 days; left chest, back, upper abdomen	0	0	Generalized rhonchi 1st day; consolidation right base 4th day; resolving consolidation left base 14th day	Bilateral midzone opacities right>left, 4th day; opacity left base 14th day
21	Mortar bomb; 3 yards Crouching	0	10 days; upper back	0	0	Cyanosis, scattered creps. both lungs 1st and 2nd days; dullness and diminished B.S. at left base 9th day	Increased density left lower zone 9th day; nil 11th day

fourteen days after wounding. The sources of injury were hand grenades, mortar bombs, land mines, aerial bombs, or flying bombs. More than half of the patients were unconscious for varying periods after operation. However, none complained of headache or showed signs of central nervous-system injury. Dyspnea as a symptom was manifested by all of them. Pain was of two types, either retrosternal or muscular, involving the intercostal muscles, the muscles of the upper abdomen, or those of the back. All but 2 patients suffered from a frothy cough. Hemoptysis occurred in three-fourths of the cases and showed an inverse relationship of this symptom to the incidence of massive hemorrhage as shown by x-rays. Generalized rhonchi were usually heard after the injury, but dullness, diminished breath sounds, and decreased fremitus depended on the degree of lung hemorrhage. Two patients were found to have a hemothorax. Roentgenograms of the lungs were negative in 10 patients examined shortly after injury. When positive roentgenograms were obtained there was nothing roentgenologically specific. The lesions were either unilateral or bilateral. Opacities were found in the middle or lower zones and were centrally placed. There was no correlation between the severity of the symptoms and the amount of pulmonary damage as revealed by the x-rays. The treatment for blast injury of the lung was symptomatic. The use of sulfonamides prevented pneumonia.

BENJAMIN G. P. SHAFIROFF, M.D.

Pillsbury, N. R., and Wassersug, J. D.: The Differentiation of Bronchiogenic Carcinoma and Pulmonary Tuberculosis. *N. England J. M.*, 1945, 232: 276.

Because of the many clinical and roentgenological similarities of bronchiogenic carcinoma and pulmonary tuberculosis, their differentiation may present certain diagnostic difficulties. Twelve proved cases of bronchiogenic carcinoma which were admitted to a tuberculosis hospital are presented by the authors.

Patients with bronchiogenic carcinoma are occasionally admitted to a sanatorium, either for observation for tuberculosis or because a definite diagnosis of tuberculosis has already been made. Since the clinical findings may be misleading, reliance must be placed on other diagnostic aids, such as x-ray examination, bronchoscopy, and exploratory thoracotomy.

Bronchiogenic carcinoma must be promptly differentiated from tuberculosis, since time and rest never cure a malignant growth. Waiting six weeks or longer for results of animal inoculation tests or cultures of sputum may rob the patient of his chance of surgical cure.

An early diagnosis of bronchiogenic carcinoma can be made only if the disease is suspected and considered in the differential diagnosis. The possibility of cancer must be given special consideration if the patient is a man between forty and sixty years of age. In all cases in which thoracic symptoms are present, x-ray examination of the chest should be made immediately. If, on the basis of physical and x-ray examination, the disease cannot be differentiated from pulmonary tuberculosis, and a few specimens of sputum are negative, bronchoscopy should be performed without further delay. Inspection of the bronchi, if the patient's general condition admits it, yields valuable information that may determine not only the diagnosis but also how the case is to be managed. This is as true in pulmonary tuberculosis as it is in bronchiogenic carcinoma, since the presence or absence of endobronchial tuberculosis may alter the plans for collapse therapy. Hence, in either disease much may be gained by prompt bronchoscopic examination.

In the authors' series, all the patients were men, and all were between forty and sixty-eight years of age at the time of their admission to the sanatorium. In 9 of the 12 cases, the disease was in the right bronchial tree. All the patients had a productive cough, but neither the character of the cough nor the gross appearance of the sputum was distinguishable from that found in many other pulmonary disorders. Dullness of some degree and alteration in breath sounds were noted in every case. Rales, often apical, were detected in 8 cases. In one-half of the cases in the present series, cavitation was shown on the admission x-ray films. It is important to remember that a negative roentgenogram does not definitely rule out the presence of carcinoma. If symptoms are suggestive and persistent, a negative roentgenogram should not deter one from further diagnostic studies. To be of value from a therapeutic standpoint, bronchoscopy must be performed early in the course of the disease.

JOSEPH K. NARAT, M.D.

Holinger, P. H., Hara, H. J., and Hirsch, E. F.: Bronchogenic Carcinoma; An Analysis of 175 Proved Cases. *Ann. Otol. Rhinol.*, 1945, 54: 5.

The authors present a comprehensive study of 175 cases of proved carcinoma of the bronchus. It is generally recognized that there has been not only an apparent, but also an actual numerical increase in the incidence of this disease. Improved methods of diagnosis and a greater interest on the part of the profession have contributed much toward its early recognition. Bronchogenic carcinoma is fifth in frequency in carcinoma among males.

As in cancer of other parts of the body, nothing definite is known of its etiology, but it is generally agreed that a chronic irritant is an essential common factor. It occurs more frequently in the male, and the ratio is sometimes as high as 9 to 1.

Pathologically, practically all carcinomas of the lung arise in bronchial tissue, and in the majority of cases the lesion is found in the right bronchus, at or near the hilum.

The authors state that the onset is usually insidious and that patients often are unable to state the exact date of the onset of symptoms.

In order of frequency, the symptoms in this series were cough, cold, suspected tuberculosis, thoracic pain, pneumonia, influenza, and weakness.

Physical signs are usually absent in the early stages. Roentgenologically, there is extreme variation in the findings. No single finding or group of findings can be considered pathognomonic, but x-ray examination must be considered to be the most accurate of the procedures which lead to a presumptive diagnosis of this disease.

Bronchoscopy should be done in all patients with obscure pulmonary pathology, in the hope of removing tissue for biopsy. This procedure has been successful in approximately 80 per cent of the cases.

In the series of cases reported, squamous-cell carcinoma was the predominating type and comprised 64 per cent of all the carcinomas: small round-cell carcinoma in 17 per cent; anaplastic in 13 per cent; and adenocarcinoma in 6 per cent.

The treatment is primarily surgical, although other methods of treatment are sometimes used, such as surgical diathermy and the direct implantation of radon seeds or radium into the tumor. These methods are not suggested as of value in cases considered operable. JOHN F. DELPH, M.D.

HEART AND PERICARDIUM

Batchelor, T. M., and Maun, M. E.: Congenital Glycogenic Tumors of the Heart. *Arch. Path.*, Chic., 1945, 39: 67.

Congenital tumors of the heart (rhabdomyomas) are comparatively rare. Since von Recklinghausen described the first case in 1862, 62 authentic cases have been recorded. The cardiac tumors were seen chiefly in infants and the newborn, with 52 per cent of the patients dying in the first year of life and 86 per cent before they reached puberty.

Glycogen tumors of the heart rarely cause clinical symptoms except in those patients in whom the tumors are situated on the valve leaflets; in the event of this location murmurs may be heard. Cyanosis was a frequent symptom in the cases reviewed, especially in the newborn infants and in those patients who died suddenly. Since tuberous sclerosis was associated with congenital nodular cardiac tumors in 50 per cent of the cases, one would expect symptoms of a neurological nature; such symptoms occurred. In children and infants the mental development was retarded, and the ability to walk and talk was delayed; some of the patients exhibited marked indifference to their surroundings. In some of the patients, epileptiform attacks were frequent. However, one of the most constant findings was the occurrence of sudden death after minor ailments from which recovery was usually expected. In no case was the diagnosis made before death.

The case reported by the authors is the eleventh in American literature and the sixty-third in the general medical literature. In a case of multiple tumors of the heart in a three-day-old boy, glycogen was demonstrated within the tumor cells.

The authors suggest that the term "congenital nodular glycogenic tumors of the heart" should replace "congenital rhabdomyoma" until more is known about the nature of the lesions.

JOSEPH K. NARAT, M.D.

Straus, R., and Merliss, R.: Primary Tumor of the Heart. *Arch. Path.*, Chic., 1945, 39: 74.

Reports of primary tumor of the heart appear infrequently in the literature. Because of the reluctance of many students of the subject to accept the diagnosis given in some of these reports, there has been a considerable variation in the estimate of the number of cases that have occurred, the number varying with the bias of the author. Apparently only 163 cases have been reported to date. Individual experience varies considerably, as among 30,000 autopsies no cases have been seen according to 1 report, whereas other workers have reported 3 cases of primary cardiac tumor among 1,200 autopsies.

The site of the tumor may be in practically any part of the heart, but the tumor is found less frequently on a valve and most commonly in an atrium. Apparently it may be either single or multiple. It is agreed that in all cases of tumor of the heart the neoplasm is of mesoblastic origin, and therefore it has been reported as a myxoma, fibroma, lipoma, lymphangioendothelioma, hemangioendothelioma, leiomyoma, rhabdomyoma, rhabdomyosarcoma, leiomyosarcoma, fibrosarcoma, or polymorphous cell sarcoma. According to the literature, the disease occurs twice as frequently among males as among females. The younger age group is chiefly affected, but ages have ranged from ten months to seventy-nine years.

As a rule, tumor of the heart is not diagnosed clinically. In patients, who have had a primary cancer elsewhere and subsequently showed signs of cardiac irregularity, metastatic tumor of the heart has been diagnosed. On the other hand, there are many cases of metastatic tumor of the heart that present no electrocardiographic or clinical signs. Only 2 cases are recorded in which primary tumor of the heart was diagnosed before death.

Whether or not primary tumor of the heart can be diagnosed prior to death will depend certainly on its ability to produce symptoms by interfering with the cardiac mechanism. A small, slowly growing tumor of a chamber of the heart, and in some cases a larger one in an "out of the way" position, would not be physiologically apparent. A tumor on a valve, if sufficiently large, could be expected to produce murmurs but, unless suspected, would certainly be overlooked in the differential diagnosis. A large tumor of an atrium with a ball and valve action in either the mitral or the tricuspid ring and with murmurs affected by a shift in the position of the body should certainly be amenable to clinical diagnosis if kept in mind. In regard to cancer, the signs and symptoms most likely to be produced would be hemorrhagic pericardial effusions due to

pericardial involvement, interference with the conduction system from an infiltration of the myocardium, murmurs when the valves are involved, and if the tumor is friable, distant metastases and possibly emboli. At times the roentgenogram may be of assistance, particularly when a large bulky tumor produces gross changes in the shape of the heart or an intravenously injected radiopaque dye outlines the chambers of the heart. All cardiac tumors are usually characterized clinically by a sudden onset of severe cardiac failure without any apparent etiological or anatomic basis, and a fairly rapid downhill course.

Of the 3 cases of primary tumor of the heart reported by the authors, 2 were instances of myxoma and 1 was a case of myxosarcoma. In 2 cases the tumor was silent, while in the third case it produced clinical signs and symptoms of tricuspid stenosis.

The sudden onset of signs of cardiac decompensation in a young person without a pre-existing history of cardiac disease and with no discoverable anatomic basis for the cardiac disease, a hemorrhagic pericardial effusion, sometimes an involvement of valvular function or of the conduction system, and signs of valvular stenosis which change on motion of the body, as well as signs of mediastinal tumor with alteration of the appearance of the shape of the heart in the roentgenogram, should cause one to consider primary tumor of the heart in the differential diagnosis of the condition under examination.

JOSEPH K. NARAT, M.D.

Watts, T. D., and Toone, E. C.: Successful Removal of a Foreign Body within the Pericardium. *Surgery*, 1945, 17: 454.

The authors report the case history, operative record, and postoperative course of a soldier who was hospitalized because of disabling recurrent attacks of pain in the left shoulder and left chest. In March, 1943 he was wounded by a shell fragment which entered the left anterior chest at the level of the third intercostal space just lateral to the sternal border. He was apparently unconscious for twenty-four hours. He complained of dull substernal pain which became sharp and severe with deep breathing or coughing. These symptoms disappeared spontaneously. He was discharged from the hospital twenty-six days later, but the pain recurred sixteen days after he had left the hospital. This pain originated in the supraclavicular region of the left shoulder and radiated to the left chest anteriorly. The attack disappeared spontaneously only to recur three times during the next two months.

He was again hospitalized in August, 1943 because of his inability to perform the duties of a combat soldier. At this time he was observed while having 2 severe attacks of pain. X-ray examination revealed a small metallic foreign body lying adjacent to the base of the heart in the region of the right auricle, and a small healed scar (1 by 1 cm.) in the third left intercostal space adjacent to the sternal border. The electrocardiogram indicated myocardial damage. The general examination was essentially negative.

Under combined local and general anesthesia, a right parasternal incision was made from the lower border of the second rib along the sternal margin to the fifth rib and to the nipple line. The costal cartilages were resected. The internal mammary vessels and intercostals were ligated. It was also necessary to resect a portion of the sternum. The pericardium was opened, to expose the right ventricle, right auricle, and superior vena cava. There were many adhesions present, which were separated, and a foreign body approximately 1 cm. long was found encapsulated on the anterior aspect of the right auricle close to the superior vena cava. The fragment was freed and removed.

Postoperatively there was some precordial pain and pulse irregularity, together with some cyanosis. A small area of atelectasis developed in the right base, which cleared. There was superficial wound infection in spite of chemotherapy. This infection was drained. A friction rub on the right developed on the ninth day and this, too, cleared in forty-eight hours. The patient was discharged in good condition on November 16, 1943.

BENJAMIN GOLDMAN, M.D.

Wise, A. W., and Shafer, L. E.: Purulent Pericardial Effusion Treated with Penicillin Given Intrapericardially. *J. Am. M. Ass.*, 1945, 127: 583.

Wise and Shafer report a case history of a female aged thirty-one who was seen in the hospital four days after an illness of fever, cough, dyspnea, and slight hemoptysis. Physical examination suggested a tentative diagnosis of left lobar pneumonia with associated pericardial effusion. X-ray examination revealed consolidation in the left lower lobe and enlargement of the heart on both the right and left sides. The sputum could not be typed, possibly because sulfadiazine had been given for four days before admission, but numerous pneumococci were seen.

Despite the administration of sulfadiazine the patient became progressively worse. The intramuscular administration of 15,000 units of penicillin every

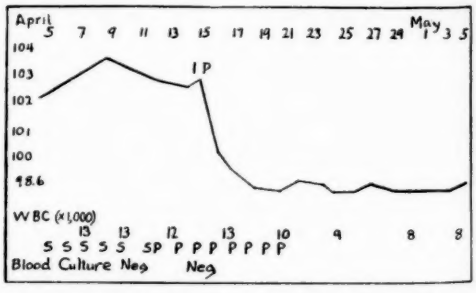


Chart 1. Clinical course. S, sulfadiazine; P, penicillin; IP, intrapericardial penicillin.

three hours for three days did not improve her condition very much. A pericardial paracentesis was then done, 70 c.c. of turbid blood-tinged fluid being removed, and 40,000 units of penicillin were injected in 30 c.c. of normal sodium-chloride solution. Within sixteen hours the temperature dropped to normal and except for an occasional flare-up continued in the same manner. The intramuscular administration of penicillin was continued in decreasing doses for four or five days. The patient was discharged as cured on her thirty-fourth hospital day.

It is the opinion of the authors that this case represents a purulent pericardial effusion secondary to lobar pneumonia which failed to respond to sulfadiazine or to penicillin given intramuscularly, but did respond dramatically when penicillin was administered intrapericardially.

BENJAMIN GOLDMAN, M.D.

ESOPHAGUS AND MEDIASTINUM

Borges, E. J.: Cancer of the Esophagus. *Ind. J. Surg.*, 1944, 6: 188.

An analysis of 153 cases of cancer of the esophagus is presented. These cases were admitted to the Tata Memorial Hospital in Bombay during the period from March, 1941 to December, 1942—twenty months. They represent 4.8 per cent of all malignancies admitted to this hospital.

The youngest patient was thirty years old; in fact, there were 19 cases in the age group between thirty and thirty-nine years. The males predominated—124 men to 29 women. There was also a marked incidence in certain communities, one-third of the total number of cases coming from one community or tribe.

One hundred and forty-one of the patients had dysphagia as the first symptom; 8 had pain as the initial symptom, and hoarseness and general debility were the first symptoms in 2 other cases. Only 55 of the total number of cases had symptoms of less than 3 months' duration.

Ninety-nine of the total number of cases had esophagoscopic examination and positive biopsies were obtained in 83. In 26 cases the lesion was above the bifurcation of the trachea, in 31 cases it was at the bifurcation, and in 69 cases it was below the bifurcation. Distant metastasis was not the rule, the lymph nodes in the posterior mediastinum and those about the left gastric artery being most commonly involved. All but 2 of the cases showed squamous or epidermoid carcinoma, there being only 2 cases of adenocarcinoma.

The author believes in radical resection whenever it is possible. There were 4 cases in which a resection and an esophagogastrostomy was done. Three of the patients died in the postoperative period and the last survived 10 months before recurrence was fatal. Four other patients had a radical resection and cervical esophagostomy; 3 of these died in the postoperative period while 1 survived the operation and died two months later of amebic dysentery.

X-ray therapy may be helpful in some cases as it decreases the edema about the tumor, although in some cases it seems to increase the edema and necessitates an earlier gastrostomy.

FORREST D. DODRILL, M.D.

Tomlinson, W. J., and Wilson, L. A., Jr.: Esophageal Carcinoma in British West Indian and Panamanian Negroes; A Study of the Incidence, Etiological Factors, and Pathological Anatomy in 50 Cases. *Arch. Path.*, Chic., 1945, 39: 79.

In recent reports of esophageal carcinoma it has been suggested that this tumor is far more frequent in white males, especially in those of Jewish extraction, than in West Indian and Panamanian negroes. The authors are presenting the data from complete autopsies in 50 cases of esophageal carcinoma occurring in negroes, indians and mestizo persons of British West Indian and Panamanian races. Forty-five were men and 5 women. The tumor was located in the upper third of the esophagus in 5 instances, in the middle third in 25, and in the lower third in 22.

Of the 50 persons with esophageal carcinoma, 26 had clinical and autopsy evidence of syphilis and 22 had no recognizable syphilis. A decision could not be made in regard to the remaining 2. The average incidence of syphilis in the entire autopsy population for the past ten years is 8.7 per cent.

In the 50 cases of esophageal carcinoma studied, the periesophageal lymph nodes were grossly invaded in every instance.

In British West Indian negroes, carcinoma of the esophagus ranks third as to the number of cases among all the types of carcinoma observed at autopsy.

JOSEPH K. NARAT, M.D.

SURGERY OF THE ABDOMEN

ABDOMINAL WALL AND PERITONEUM

Mair, G. B.: Preliminary Report on the Use of Whole-Skin Grafts as a Substitute for Fascial Sutures in the Treatment of Hernias. *Brit. J. Surg.*, 1945, 32: 381.

The author uses whole-skin grafts for cases of hernia in which fascia was formerly indicated for suture. Hitherto cutis grafts were used. Cutis contains all the elements of the skin except the epidermis. It is elastic, inherently active, and composed of a rich network of connective-tissue fibers. After transplantation, according to Uihlein (1939), these inherent factors persist in the metamorphosis of the graft, and because of the stimulus initiated and maintained by the tension under which the graft is sutured, a metaplasia into stout connective tissue takes place. The author states that the danger of epidermoid cyst formation is negligible when the cutis graft has been inlaid under tension.

The question arose in the author's mind as to whether it was really necessary to remove the epidermis, and with that end in view he investigated the use of whole-skin implants where fascia otherwise would have been used. His experimental work reveals that after several weeks, sebaceous glands, hair follicles, and epidermis had entirely disappeared; that the hairs had been surrounded by a massive foreign-body reaction; and that the hairs and the reactive tissue were in turn being encapsulated by a firm fibrous stroma.

The author has used whole skin grafts in 89 cases of different types of hernia with satisfactory results. However, insufficient time has elapsed to evaluate the recurrence rates accurately. JOSEPH GASTER, M.D.

GASTROINTESTINAL TRACT

Taylor, H.: An Operation for Removal of Carcinoma of the Esophagus with Presternal Esophagogastrostomy. *Brit. J. Surg.*, 1945, 32: 394.

In this article an operation is suggested in which an esophageal or gastroesophageal resection of a growth is followed by a presternal or suprasternal anastomosis between the stump of the esophagus and the stomach or the remaining part of it. Such a procedure is, of course, a formidable undertaking, but this is a consideration which must be viewed against the hopeless and distressing alternative for a patient with a growth of the esophagus or cardia.

The operation has been put into practice in 3 cases, with 1 death from accidental pneumothorax of the opposite side of the chest, 1 death from empyema after eight months, and 1 living patient, who is taking soft food by mouth and enjoying her life at home eighteen months later.

Preoperative preparation consists in rest in bed for from two to four weeks with a high caloric fluid diet by mouth, unless obstruction is absolute. This period is used to remove all septic foci in the mouth, to reduce esophageal stasis by regular lavage with an esophageal tube, and to give a blood transfusion if required. Esophagoscopy is essential to confirm the diagnosis by inspection and biopsy. It may also provide evidence of fixity of the gullet in the mediastinum or, with bronchoscopy, involvement of the trachea or left bronchus, which would, of course, contraindicate operation. At the same time it affords an opportunity of dilating the stricture, if necessary, to facilitate feeding and esophageal drainage.

Shortly before operation a course of local chemotherapy is instituted in which the lavage after each feeding is followed by a dose of sulfathiazole suspension in order to reduce the infection of the growth. Breathing exercises are instituted and the patient is familiarized with the oxygen mask in preparation for the postoperative period. Preliminary jejunostomy is not necessary if there has been a good response to these measures, but it may be required if the esophageal obstruction has not sufficiently diminished under treatment.

Cyclopropane and oxygen administered by a cuffed endotracheal tube is the method of anesthesia adopted in order to give the anesthetist unhampered control of respiration by means of positive pressure when the chest is open and the physiological mechanism for expanding the lung cannot function. The operation commences with the setting up of a drip transfusion of blood, followed later by plasma, while, in anticipation of a lengthy dissection, measures to keep the patient warm are taken from the outset, and pulse-rate and blood-pressure readings are taken at fifteen-minute intervals.

The procedure for a growth in the upper half or two-thirds of the esophagus will first be described. For this, a right thoracotomy is chosen in order that the dissection in the region of the aortic arch may proceed more readily under vision. The patient is therefore placed in a half-left lateral position and his right arm is supported by an assistant, as it will be necessary to move it during the operation. The right pleural cavity is opened through the bed of the sixth rib and any parietal adhesions of the lung are separated until it lies on the mediastinum and the growth in the esophagus is exposed. If there is no obvious infiltration of the mediastinum and the pleural covering is incised, the azygos vein is divided, and the growth is gently dissected free, care being taken to avoid tearing the left pleura below. Even with positive pressure in the trachea such a tear may have a valvular action, and if it occurs there is danger of a contralateral pneumothorax with obstruction of the pulmonary blood flow and general circulatory failure. The opening should therefore be carefully sutured, but if this is not possible a vent

tube should be put through it until the end of the operation, to prevent any possibility of valve action and to allow the anesthetist to keep the lung fully expanded. While the mediastinal dissection is proceeding, in fact as soon as it has been decided that the condition is operable, an independent assistant makes two other short incisions. The first, about 1½ inches long, is made into the peritoneal cavity through the midline of the epigastrium and the wound is covered with a towel until it is required. The second incision, about 1 inch long, is made transversely in the skin over the suprasternal notch. Through this opening the assistant tunnels downward in the relatively bloodless subcutaneous tissue in front of the sternum, by the method of repeated scissor-spreading, as far as the length of the scissors will allow. This tunnel will eventually accommodate the upper stump of the esophagus, and if it is prepared in advance in this way much time will be saved in the later maneuver.

Meanwhile, within the chest, the surgeon completes the mobilization of the whole length of the esophagus by freezing the two ends. Below, the attachments of the cardia are separated from the esophageal hiatus of the diaphragm, the peritoneal cavity being deliberately opened anteriorly. Above, the loose cellular tissue at the root of the neck strips easily from the esophagus until the cricoid is reached. Great gentleness is required here to avoid damage to the important descending esophageal branches of the inferior thyroid arteries. When the esophagus is quite free from the cricoid to the stomach, a special long curved clamp is introduced into the epigastric incision and, passing between the stomach and the left lobe of the liver, is guided by the surgeon's fingers through the peritoneal opening which was made at the esophageal hiatus of the diaphragm, continued high into the chest, and clamped across the esophagus above the growth. The first two fingers of the surgeon's left hand now slide up the esophagus to the cricoid and work their way forward in the neck between the pharynx and the right carotid sheath until they present at the assistant's suprasternal incision which is also the mouth of the subcutaneous tunnel. This maneuver is illustrated in the diagram for greater clarity. The fingers guide the blades of a second clamp from the cervical incision down into the chest, where they are applied to the esophagus immediately above the first clamp. The esophagus is then divided between the clamps, which are immediately withdrawn to the exterior, carrying the two parts of the esophagus with them. The lower part is carried through the diaphragm and out of the epigastric incision; the upper part is drawn through the root of the neck to the space of Burns, whence it is thrust down the presternal tunnel as far as it will go. The assistant completes the cervical part of the operation by bringing the end of the upper part of the esophagus out through a short counterincision over the tunnel, after which the suprasternal incision, having served its purpose, is sutured. The edges of the esophageal opening in the

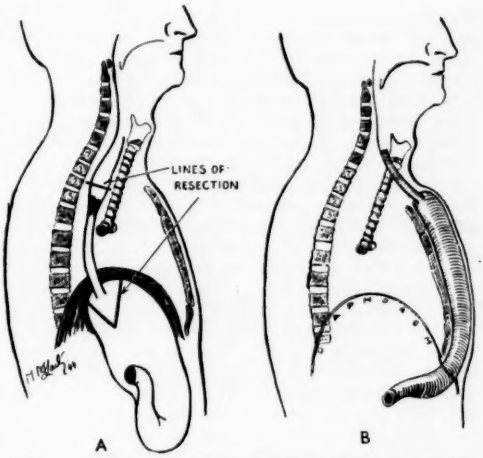


Fig. 1. Diagrammatic representation of the operation. A, Shows the gastroesophageal resection; B, shows the remainder of the stomach brought upward to the front of the sternum and anastomosed to the stump of the esophagus.

diaphragm may be approximated if necessary, after which the mediastinum is dusted with sulfonamide powder and the thorax is closed with underwater drainage. Dressings are applied, the lung is expanded by the anesthetist, and the patient is slowly placed on his back.

The first stage of the operation having now been completed, the general condition of the patient is critically reviewed by the surgeon and the anesthetist, to decide whether it is possible to proceed at once to the mobilization of the stomach into the presternal position. If the anesthetist's chart indicates a progressive fall of blood pressure, especially if the systolic reading is below 100 mm. of mercury, the second stage should be postponed until a later date. In case of doubt, the patient's response to an interval of ten-minutes' rest is a useful indication of the degree of reserve vitality he possesses.

If it is considered wise to desist, the upper end of the esophagus is sutured to the opening in the presternal tunnel, the growth is removed from the lower esophagus and this end is sutured to the skin of the epigastrium. In the interval before the second stage the patient will be fed through the lower esophagostomy and later the two fistulas may be temporarily connected by an external tube, as in Torek's case. The second stage, can, however, be fairly rapidly performed and it is very desirable to avoid the epigastric fistula if possible. If, therefore, it is decided to proceed at once to the anastomosis, the epigastric incision is enlarged and the presternal subcutaneous tunnel is extended downward to join it. The stomach is now mobilized by gentle traction on the esophagus, which facilitates the division of the root of the coronary vessels beyond the glands in

this region, as well as the vasa brevia to the spleen and the great omentum along the greater curve. This can be done without visible impairment of the blood supply of the fundus of the stomach if care has been taken to avoid damage to the pyloric and right gastroepiploic vessels. It will now be found that the stomach can be withdrawn entirely from the abdomen and laid on the front of the chest with the fundus as high as the sternal angle of Ludwig. By mobilization of the duodenum as well, it can be drawn even higher so that the pylorus lies over the xiphisternum and the fundus reaches above the clavicle. This degree of mobilization is necessary only after a very high resection of the esophagus, but enough of the stomach is freed to allow the fundus to reach the upper end of the esophagus without tension. The growth, with the lower esophagus, the cardia, the upper part of the lesser curve, and the glands which have been dissected up from the celiac axis are now removed, and the opening in the stomach is closed in two layers. The fundus is drawn up the presternal tunnel to the counter incision for the anastomosis, while the assistant closes the epigastric wound, taking care to leave plenty of room for the stomach to pass between the muscles without constriction. The fundus is sutured to the chest wall about 1 inch higher than the upper end of the esophagus, which is laid on its surface and sutured in position. A small incision is now made into the stomach wall opposite the end of the esophagus and an anastomosis is made between the two openings, the suture line being covered by drawing the anterior wall of stomach up over it. The skin over the anastomosis is closed with drainage of the subcutaneous tissue and the operation is completed by passing a small nasal tube through the anastomosis into the presternal part of the stomach.

When the operation is performed for growths of the lower part of the esophagus or of the cardiac end of the stomach, the exposure is through the bed of the seventh left rib, the diaphragm is incised radially from the esophageal hiatus, and the growth is dissected free. Therefore, the first steps are those of Sauerbruch's operation, which will be the method of choice if the growth is limited to the cardia or does not extend higher than the concavity of the aortic arch. The surgeon may well defer the selection of an intra- or an extrathoracic anastomosis until, with the parts in his hands, he is in a position to assess the practicability of the former. If this is not possible he need not abandon the resection, but may proceed to apply the principle of the operation described above with sufficient modification to conform to the anatomy of the aortic arch. Thus the esophagus must be freed by blunt dissection with the finger between the deep side of the arch and the azygos vein after this region has been infiltrated with ½ per cent novocain. The dissection of the root of the neck is to the left of the trachea, and when the esophageal clamp is passed down from the neck into the chest it must follow the same path between the azygos vein and aortic arch before it is applied to the lower esophagus and withdrawn.

The blood supply of the esophagus is more precarious when it is divided low down, and particular care must be taken in dissecting the root of the neck not to damage the vessels joining the upper end from the inferior thyroid trunks. It is expedient also to extend the incision across the costal margin and left rectus muscle to the epigastrium to obtain a wide thoracicoabdominal exposure for the dissection of an extensive growth in the stomach. The spleen and proximal omentum should be removed with the growth, and the stomach divided about halfway down the greater curvature and as far as the incisura on the lesser curve. Case 3 shows that this degree of removal of tissue is still compatible with a presternal anastomosis if the duodenum is mobilized as well as the stomach. Apart from the approach and exposure, and the dissection below the diaphragm and opposite the aortic arch, the execution of the operation follows the same lines as that described for upper esophageal resection.

During the postoperative period the patient is sustained by fluid diet through the nasal tube, through which sulfathiazole suspension is also administered. When not used for this purpose the tube is kept open to the atmosphere to prevent gas distention of the stomach and thus remove any internal strain on the anastomosis. Leakage here is fraught with danger of widespread infection of the subcutaneous tissue in front of the chest and a careful watch must be kept to prevent this. The integrity of the suture line may be tested by a drink of methylene blue which will ooze from the local drainage tubes if the suture is not sound. Continuous suction to remove escaped saliva may prevent a complete breakdown, but if inflammation is spreading it is better to limit this by opening up the wound and intubating the fistula. If the anastomosis holds, nothing is allowed by mouth until the esophagus and stomach are firmly adherent in their new position, but mouth washes may be freely used. Sips of fluid may be given on the seventh day and the nasal tube is removed on the tenth day if all is well. The underwater drain is removed when the discharge has ceased to be copious, but the residual pleural fluid is aspirated at intervals and cultured. Penicillin may be injected at the same time to minimize the risk of secondary infection from the bronchopneumonic lung. BENJAMIN GOLDMAN, M.D.

Christiansen, T.: Postoperative Gastritis. Gastroscopic Examinations (Ueber postoperative Gastritis. Gastroskopische Untersuchungen). *Acta med. scand.*, 1943, 115: 496.

Postoperative gastritis is a special form of gastritis, differing from other forms in its clinical picture as well as in its pathological and gastroscopic aspects. Gastroscopy reveals a very polymorphous picture which is characterized by a mixture of superficial, hypertrophic, atrophic, erosive, and ulcerative lesions. The clinical symptoms differ in many re-

spects from peptic ulcer, for instance, the pain is not relieved by food intake. The question of pathogenesis is open to argument, and different theories are discussed.

European and American authors differ in their opinions concerning the frequency of the disease. In Europe, it is considered as being extremely frequent, whereas American workers (Eusterman and Balfour, Mayo Clinic) believe it to be rare. The author tries to account for this divergence of opinion by the fact that the European writers base their diagnosis upon gastroscopic findings whereas in America the diagnosis is based on clinical symptoms.

Ten case histories are reported and discussed; 5 of the cases occurred after gastroenterostomy and 5 after resection. The patients developed clinical symptoms of gastritis from two to thirty years after the operation. In 9 of the cases gastroscopy revealed a typical gastritis, whereas in 1 case only, no gastritis was found by gastroscopy. The lesions were localized mostly at the stoma and at the anastomosis of the intestine. There may or may not be free hydrochloric acid. The prognosis is poor.

Although some clinical improvement was achieved by a combination of the Sippy treatment and daily gastric lavage, no improvement of the gastroscopic findings could be observed after the treatment. Mucine treatment seemed to be ineffective.

WERNER M. SOLMITZ, M.D.

Price, P. B., and Lee, T. F.: The Use of Omentum to Close Perforations of the Stomach. *Arch. Surg.*, 1945, 50: 171.

It is common practice to cover perforated ulcers of the stomach with tabs of omentum, especially when the adjacent gastric wall is too indurated and friable for satisfactory closure of the hole with sutures alone. Free omental transplants, or grafts, have been recommended for this purpose, but on theoretical grounds it may be questioned whether this procedure is sound surgical practice. One might expect the free transplants, deprived temporarily of a blood supply, to be susceptible both to the digestive action of gastric juice and to infection, which is sure to be present, at least part of the time. In this case the safer procedure would be to cover the defects with only living omentum, which presumably would offer greater resistance to both digestion and infection.

The authors have studied this problem experimentally on dogs. With aseptic technique, round or oval holes were cut in the anterior gastric wall. The holes were deliberately made larger than the perforations encountered clinically because it was desired to subject the covering omentum to relatively severe tests, and also because small holes in the normal gastric wall heal too rapidly to present the problems posed by the more slowly healing perforations of peptic ulcer. Cotton thread was used for sutures and ligatures. All the animals were allowed water and food (dog pellets) ad libitum after operation.

Living omental patches or tabs were used successfully to cover relatively large holes in the stomachs of dogs. Such seals appeared to be highly resistant to digestion and infection, and gave the gastric defects time to heal.

On the other hand, free omental transplants similarly employed, being temporarily without any blood supply, were found to be susceptible to infection and the corrosive action of gastric juice. Necrosis and perforation of the graft occurred in many instances.

These experimental results suggest that in clinical surgical procedures it is more rational and safer to use living tissue than free omental grafts to cover perforated gastric ulcers or to re-enforce lines of anastomosis.

JOSEPH K. NARAT, M.D.

Custer, W. C.: Survival after Gastric Resection in Carcinoma of the Stomach. *Surgery*, 1945, 17: 510.

Over a fourteen-year period, exploratory laparotomy for carcinoma of the stomach was performed on 463 patients. Of these, 141 were considered to have operable lesions and gastric resection was performed. The follow-up clinic was able to carry through a study in 96 cases, which can be classified as follows:

	Number	Per cent
Operative deaths	2	2.03
Fatal postoperative complications	9	9.37
Deaths under three years (not including above)	23	23.95
Patients failing to live over three years	34	35.34
Deaths in the three-to-five-year interval (5 patients died of other causes and had no evidence of recurrence)	36	37.59
Deaths in the five-to-eight-year interval (2 patients died of other causes and had no evidence of recurrence)	8	.....
Patients alive and well for over eight years	18	18.75

To summarize, there were 141 patients with an established diagnosis of carcinoma of the stomach on whom gastric resection was performed. After five years, 27.06 per cent were alive, and after eight years, 18.75 per cent were still living. In contrast, there was a group of 28 patients in whom the diagnosis of operable gastric cancer had been made who refused surgery. The mortality of this group of patients was 100 per cent at the end of three years.

JOHN L. LINDQUIST, M.D.

Engel, G. C.: The Creation of a Gastric Pouch following Total Gastrectomy. *Surgery*, 1945, 17: 512.

This report deals with one of the problems following total gastrectomy, namely, the inability of some patients with an esophagojejunostomy to handle even small feedings without a feeling of fullness and discomfort because of the lack of physical space in the jejunum to accommodate a moderate-sized meal. The symptoms of distress in the case presented were not due to contracture, stenosis, or spasm of the esophagojejunal anastomosis; they were relieved by a secondary operation creating a pouch out of the efferent and afferent loops of jejunum. The patient was a fifty-seven-year-old man who had a large peptic ulcer on the lesser curvature of the stomach involv-

ing the lower 1.3 cm. of the esophagus. Because of the induration of the rest of the stomach and an associated gastritis it was decided that total gastrectomy was indicated.

The reflection of the diaphragmatic peritoneum was freed where it overlies the esophagus. The anastomosis of the esophagus to the jejunum was done after the method of Lahey with a long jejunal loop brought up anterior to the transverse colon. The great omentum was amputated to prevent drag on the afferent jejunal loop. A Jutte tube was passed down the esophagus and into the efferent loop of jejunum for postoperative feeding. The tube was removed on the sixth day and the patient was on a soft diet on the seventeenth day. The patient complained of fullness and distress after eating. A barium x-ray film showed the anastomosis to be functioning and of normal size. The complaint and symptoms of distress continued, and on the twenty-eighth postoperative day it was decided to reoperate and make a pouch out of the afferent and efferent loops of jejunum. This was done by creating an anastomosis between the two loops of jejunum in a manner similar to that employed in the Finney gastroduodenostomy. The patient had an uneventful convalescence and six months later was able to eat a full diet of three meals daily.

The author describes another case of total gastrectomy for carcinoma of the stomach in which the procedure was carried out at the same stage as the resection. JOHN L. LINDQUIST, M.D.

Acebal, J. A.: The Treatment of Perforated Ulcers of the Stomach and Duodenum (Tratamiento de las ulceras perforadas del estomago y duodeno). *Rev. med. Rosario*, 1945, 35: 1.

Perforation of an ulcer of the stomach or duodenum results in generalized peritonitis and death of the patient unless an operation is performed. Some authors report cases of spontaneous recovery without operation but these are probably cases of covered ulcer, and it is impossible to tell in advance what the course will be. Therefore, the author believes emergency operation should be performed in every case not later than twelve hours after the perforation. The time was formerly set at six hours, but it was found that operation can be performed successfully after as long as twelve hours.

The author immediately gives 1 c.c. of morphine or scopolamineukodal to relieve the pain and prepare the patient for anesthesia. Spinal anesthesia is the preferred form and was used in 20 (64.5 per cent) of the 31 cases reported without any bad results. A median supraumbilical incision is used, and the fluid is removed from the peritoneal cavity by aspiration and with compresses. Drainage is not used after operation because the drain acts as a foreign body and increases the danger of infection. After operation a most careful diet should be observed for from forty-eight to seventy-two hours until the intestinal peristalsis is re-established. To supply the loss of fluid physiological salt solution or isotonic glucose solution is given. For ileus, hypertonic salt solution is given intravenously, 30 c.c. two or three times a day. To patients in very poor general condition blood transfusions are given. The author does not resort to auscultation of the stomach after gastrectomy unless it is indicated by frequent and intense vomiting.

There has been a great improvement in the results of surgery in this condition in recent years. In 1897 the mortality was 68 per cent, according to Mikulicz, while at present it is found to be only about 20 per cent.

Tampon and suture, and complementary gastroenteroanastomosis are the conservative operations. The radical operation of gastrectomy not only treats the perforation but the disease which caused it. The choice between conservative and radical operation depends on the time elapsed since the perforation and the patient's general condition. If the fluid is copious and frankly purulent, resection is contraindicated. Resection is difficult in cases of ulcer high up on the lesser curvature or ulcer low in the duodenum with a large inflammatory tumor. The choice between conservative and radical operation must be made in each individual case according to the circumstances. About 60 or 70 per cent of the cases can be treated by gastrectomy. Among the author's cases gastrectomy was performed by the author in 16 cases; suture in 14, and suture with complementary gastroenteroanastomosis in 1 case. There were 4 deaths: 1 in a case operated on twenty-four hours after perforation; 2 in cases operated upon after eight hours; and 1 in a case operated upon after thirteen hours. Death occurred in 2 cases of ulcer of the stomach, 2 cases of ulcer of the duodenum, 3 cases of suture, 1 case of supplementary gastroenteroanastomosis, and in no case of gastrectomy. AUDREY G. MORGAN, M.D.

Bisgard, J. D.: Gastric Resection for Certain Acute Perforated Lesions of the Stomach and Duodenum with Diffuse Soiling of the Peritoneal Cavity. *Surgery*, 1945, 17: 498.

Contrary to general opinion, there is a high incidence of recurrent ulcer symptoms following simple closure of acute perforated lesions of the stomach and duodenum. The advocates of primary emergency resection for the treatment of acute perforated lesions contend that not only is the immediate mortality less or no greater than that of primary closure, but that the operation is curative rather than palliative. The author believes that both procedures have a definite place in the management of acute perforation, but that the immediate interest of most patients is best served by simple closure of the perforation, and that the high incidence of recurrence should not be a deterrent. The recurring ulcers requiring subsequent resection can be treated by elective operation with less risk.

There are a few cases, however, in which primary resection is either the operation of choice or is definitely imperative. The author presents these indi-

cations with illustrative cases. The indications for primary resection are:

1. Perforated carcinoma of the stomach with delimited resectable lesions
2. Perforated peptic ulcers associated with recent or simultaneous gross hemorrhage
3. Perforated peptic ulcers associated with fixed pyloric obstruction
4. Recurring perforations
5. Perforations with insignificant soiling
6. Very early perforation occurring in the very young

Probably under no circumstances should resection be undertaken unless the patient is in fair condition, preferably young, and the perforation of not over twelve hours' duration.

Acute perforation of a carcinoma of the stomach into the free peritoneal cavity is not common but the author was able to collect 217 cases from the literature in which the diagnosis had been established at operation or postmortem examination. In only 7 of the 217 cases was it alleged that a correct diagnosis had been made prior to operation or postmortem examination. More astonishing was the frequent failure to recognize at operation that perforation had occurred in a carcinomatous crater instead of a benign peptic ulcer. This would indicate that many of the carcinomas which perforate are small and relatively confined lesions presumably suitable for resection. The two most important problems relating to perforated carcinomas of the stomach are, first, recognition of the carcinoma by routine biopsy, and, second, operative management. In approximately 50 per cent of the cases a hopeless situation exists because of advanced peritonitis from septic soiling or delayed intervention, or because the tumor is not resectable. The difficulties of simple closure of these perforations by suture is apparent. It is the author's opinion that the hazard of gastrectomy in the presence of a diffusely soiled peritoneal cavity has been grossly overestimated and the hazard of leakage from a sutured perforation in carcinomatous tissue much underestimated.

When perforated peptic ulcer is associated with recent or simultaneous hemorrhage, the hemorrhage contributes enormously to the mortality and it appears that simple closure of the perforation is inadequate because too often it fails to control the hemorrhage. Postmortem examination has shown that these patients often have multiple ulcers and that hemorrhage usually arises from the nonperforated one. Therefore, gastric resection which removes the entire ulcer-bearing area and all sources of hemorrhage is indicated in these cases.

Repeated or recurrent acute perforations are uncommon, but patients in this category develop very acute ulcers which perforate with little or no warning and many of them have an ulcer diathesis and eventually require resection. In such cases there is adequate indication for emergency resection at the time of the second perforation if circumstances are favorable.

Most of the pyloric obstructions associated with perforation are due to inflammatory edema which rapidly subsides in most instances following operation. In a few cases the obstruction is fixed or permanent as the result of scarring. In these cases a bypass must be provided and for this purpose gastroenterostomy is a poor second choice to resection. From the evidence available in the literature simple closure of perforated jejunal stoma ulcers carries a higher mortality than either subtotal gastrectomy or disconnection of the gastroenterostomy.

The majority of patients under thirty-five years of age who suffer from acute perforation do not remain free of ulcer symptoms following simple closure and in many instances have recurrent ulceration necessitating surgical intervention. In the hands of skilled surgeons resection in these patients will be attended with little or no more primary mortality than simple closure and the percentage of permanent cures will be much higher.

From available statistical data it appears that subtotal gastric resection can be performed in the presence of diffuse soiling of the peritoneal cavity within twelve hours after the perforation of ulcerating lesions of the upper gastrointestinal tract in good risk cases with a lower mortality than that obtained by simple closure with sutures. The incidence of recurrent ulceration following simple closure is much higher than that following resection.

JOHN L. LINDQUIST, M.D.

Coller, F. A., and Vaughan, H. H.: The Treatment of Carcinoma of the Colon. *Ann. Surg.*, 1945, 121: 395.

A series of 173 patients with carcinoma of the colon who were treated by operation is reported by the authors.

Of these patients, 16.2 per cent presented lesions beyond the reach of resection, for which only palliative operations could be carried out. Resection of the primary lesion was undertaken in 83.8 per cent of the patients. Of the latter, 19 per cent had other gross metastases in the liver or peritoneum that were beyond surgical removal. Therefore, the resections in this group were palliative in nature.

In 112 patients (64.7 per cent) resection was undertaken without evidence of gross carcinomatous spread beyond the lymph nodes; in these cure might be hoped for. Death occurred in only 1 patient in the group in which there was a chance of operative cure; it occurred from advanced disease following operative attempts to remove widespread lesions. The authors believe that surgical methods must be individualized to meet the varying conditions of disease.

The two-stage operation is satisfactory in most cases of cancer of the right colon. Small lesions may be resected in one stage by the experienced operator, with brilliant results. If the lesion is fixed, infected, or extensive, and requires wide dissection with removal of the mesocolon and the abdominal wall, the value of the two-stage operation is emphasized. If

anastomosis of small to large bowel is made at the same time as the extensive resection, the fate of the function of the anastomosis is dependent upon the anastomosis plus the associated traumatic peritonitis. Intraileal decompression certainly is necessary and indicated under these circumstances. The authors believe that with a preliminary anastomosis carried out under a controlled technique, by either the open or closed method and with quick restoration of the function of the bowel through the new channel, ileus and its concomitant symptoms are reduced to a minimum. They have rarely been obliged to decompress the small intestine following ileotransverse colostomy. When this anastomosis functions, the right colectomy can be carried out with its associated traumatic peritonitis without marked interference with the function of the gastrointestinal tract. Stage operations have drawbacks because each stage carries the dangers of any operation, but the authors' experience causes them to continue to adhere to this procedure in this instance for the reasons given. The use of the transverse incision and early mobilization of the patients has cut down the hospitalization time with this two-stage procedure until the time element is no longer an argument against it.

The authors have used the open method in 52 patients and the closed or aseptic method in 68 patients. It is believed that both methods are satisfactory; peritonitis is likely to occur from any local contamination of the peritoneum attendant upon the open anastomosis. Generalized peritonitis occurs from persistent leak of an anastomosis, severe wound infection, or as a result of contamination by rare virulent organisms. The striking point of difference between the two methods is not that peritonitis is more apt to occur with one method or the other, but that with any open anastomosis there is a high risk of contamination of the abdominal wall associated with an increased risk of infection at that location.

The splenic flexure offers great operative difficulties because of the intimate relation of the lesion with the stomach and spleen. In the authors' material there were 9 patients with lesions at this site. Five of them were treated by resection with end-to-end anastomosis, without mortality. Four patients were treated by resection of the obstructive type; 1 of these died.

Of 13 patients with lesions of the descending colon, 9 were treated by resection with primary anastomosis and 4 by resection of the obstructive type. There were no hospital deaths.

In 57 patients with lesions of the sigmoid colon exclusive of lesions involving the rectum or the rectosigmoid junction, the lesions were resected by the aseptic method in 30, by the open method in 21, and by obstructive methods in 6.

The authors are convinced that the use of sulfa drugs in the peritoneal cavity is not worth while and they are likewise convinced that their use in the abdominal wall is harmful. They believe sulfasuxadine has a place in the preparation of these patients and they intend to use it in the future for this purpose.

The authors conclude from the review of their material that primary resection with end-to-end anastomosis is feasible in many patients and offers many advantages. A complementary cecostomy is a wise safeguard if a proximal vent has not been established previously. Open or closed types of anastomosis are equally suitable without danger of peritonitis unless the anastomosis breaks down. The abdominal wall is often contaminated during the operation of open anastomosis, and wound infection is greater than with the aseptic methods of union. When the abdominal wall is contaminated, delayed closure of it minimizes the chance and degree of infection. The value of the transverse incision is mentioned. None of the sulfa drugs were employed routinely, and this series may be used as a control in future evaluation of methods of treatment. The authors conclude by emphasizing the fact that the outstanding need for better results is earlier diagnosis.

JOSEPH K. NARAT, M.D.

Fisher, H. C., and Burch, J. C.: The Treatment of Acute Appendicitis. *South. M. J.*, 1945, 38: 255.

Over a period of four years, 1,494 patients were operated on for acute appendicitis at an army general hospital. The majority of them were between twenty and forty years of age. Intestinal purgation was not a factor in the morbidity of the appendicitis since self-medication did not occur. The duration of the symptoms varied from thirteen hours to an average of eighty-three hours in the perforated group. There were only 2 deaths in the entire series of patients.

Ninety per cent of the cases were of the simple acute type as based on microscopic evidence of acute inflammation. The other 10 per cent were of the perforative variety, complicated either by abscess or generalized peritonitis. One death occurred in each of the latter subgroups. Procaine spinal anesthesia was favored.

All appendectomies were done through a McBurney incision or a slight modification thereof. The incision was usually of the "high" type, beginning at the level of the umbilicus. An incision placed that high usually prevented injury to the ilioinguinal or iliohypogastric nerves. When maximum tenderness was low, the incision was placed so as to approximate the point of tenderness.

Catgut sutures were used in the first 968 cases. Later, cotton was used exclusively, except for ligating the appendix and closing the peritoneum. As a result of this change, the incidence of wound infection decreased from 3.4 to 1.1 per cent.

Extraperitoneal drainage was restricted to the walled-off abscess. Sulfanilamide was used intra-abdominally only when there was perforation of the appendix. Within eight hours after operation, patients were permitted out of bed to void. After the fourth day, the patient was ambulatory. As a result of this form of postoperative therapy, there were no

TABLE I.—COMPARATIVE MORTALITY—ACUTE APPENDICITIS

Series	Years	Simple acute Per cent	Perforative with abscess Per cent	Perforative with generalized peritonitis Per cent	Perforative with local peritonitis Per cent	All perforative Per cent
University of Minnesota Hospital Sperling & Myrich	1932–1934	0.99	6.7	43.4	9.5	
University of Michigan Hospital Coller & Potter	1931–1933	0.46	5.7		12.5	
University of Iowa Hospital Pattison, A. C.	1919–1934	0.37	8.6	43.2	4.2	
Vanderbilt University Hospital Haggard & Kirtley	1925–1935	0.15	4.2	36.9	8.1	
Cincinnati General Hospital Reid & Montanns	1934–1938	1.03	10.08	17.22		
Bellevue Hospital Slattery & Hinton	1928–1939	1.6	7.9	33.3	9.9	17.3
Johns Hopkins Hospital Stafford & Strong	1931–1939	0	7.06	14.23		
Charity Hospital, New Orleans Barrow & Ochsner	1940	0.8				27.3
Durham, North Carolina Wade	1937–1940	0	8.5	14.2		11.9
Roosevelt Hospital, N. Y. C. Smyth	1940–1942	0	0	0	0	0
Cleveland Watkins	1930–1942	.71				12.2
Brooke General Hospital Fisher & Burch	1940–1944	0	2.9	2.5		2.7

TABLE II.—APPENDICITIS—BROOKE GENERAL HOSPITAL—PATHOLOGICAL DISTRIBUTION

Appendicitis, acute suppurative simple	645	
Appendicitis, acute perforative with abscess	34	Perforative Appendicitis 73 Cases
Appendicitis, acute perforative with general peritonitis	39	
Total acute suppurative appendicitis	718	
Interval appendicitis	610	
Incidental appendectomies	154	
Carcinoid of the appendix	4	
Actinomycosis appendix	2	
Tuberculous appendicitis	1	
Decidual reaction	3	
Oxyuris in appendix	2	
Total appendectomies	1494	

complications of phlebothrombosis and pulmonary embolization. Wound healing was satisfactory and no eventrations occurred. The patients tolerated early ambulation well.

In acute perforative appendicitis, operation was deferred until resolution or abscess occurred. Surgical drainage was done only when the abscess failed to resolve. When the abscess was not in contact with the anterior or lateral peritoneum, drainage was made by a posterior extraperitoneal stab wound. Occasionally it was possible to remove the appendix within the abscess without spill. However, appendectomy was usually performed after complete recovery from peritonitis.

BENJAMIN G. P. SHAFIROFF, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Boyden, E. A., and Layne, J. A.: The Gall Bladder in Patients with Pernicious Anemia; A Study of Nonvisualization and the Rate of Emptying. *Gastroenterology*, 1945, 4: 121.

In a preliminary study the authors observed that the gall bladder was not visualized in 40 per cent of male patients with pernicious anemia as against 22 per cent as anticipated in normal male patients. In a larger series of 48 patients with pernicious anemia the gall bladder could not be visualized in 42 per cent, namely, in 8 of 23 males (35 per cent) and in 12 of 25 females (48 per cent). The expected incidence of failure of visualization for this age group was 26 per cent.

The authors examined the protocols of 105 cases of pernicious anemia among 31,311 consecutive autopsies and found that 32 per cent of the patients had had either cholecystitis or cholelithiasis, or that the gall bladder had been removed.

The rate of emptying of the gall bladder in the group that could be visualized revealed a sex difference. In the male patients the curve of evacuation was not significantly different from that of the controls. However, in the female group there was a highly significant retardation, the gall bladders having discharged an average of only 69 per cent of their contents in the first forty minutes after a standard meal, as against 84 per cent in a control series.

The authors suggest that in some cases pernicious anemia may cause a permanent narrowing of the choledochoduodenal junction.

EARL O. LATIMER, M.D.

Finney, J. M. T., Jr., and Johnson, M. L.: Primary Carcinoma of the Gall Bladder. *Ann. Surg.*, 1945, 121: 425.

The authors report 18 cases of carcinoma of the gall bladder seen in one hospital in ten years. The patients were 2 males and 16 females. The majority of them ranged in age from sixty to seventy-nine years. The survival after operation establishing the diagnosis was very short: 6 lived less than one month, 3 from one to three months, 4 from four to six months, 2 from seven to twelve months, 2 from thirteen to eighteen months, and 1 for twenty-five months.

The incidence of carcinoma of the gall bladder compared to all gall-bladder conditions for which operations were undertaken in the authors' hospital in ten years was slightly over 1.5 per cent. The mortality rate in the same series was 1.26 per cent exclusive of the carcinomas. Two carcinomas originated in gall bladders that had been drained after the removal of stones.

The authors conclude that diagnosis is difficult and treatment is rarely of value. Because of the great frequency of stones preceding carcinoma of the gall bladder (in from 75 to 80 per cent of the cases), the authors urge that the gall bladders containing stones when the diagnosis is first made, be removed.

EARL O. LATIMER, M.D.

Curr, J. F.: Complete Rupture of the Pancreas. *Brit. J. Surg.*, 1945, 32: 386.

The author gives a detailed case report of forcible compression of the upper abdomen for several seconds. The patient was able to walk to the hospital where upper abdominal pain and rigidity were observed in an exploratory laparotomy six hours after injury. At operation there was a tremendous amount of fresh blood in the peritoneum. There was a 3-inch tear in the transverse mesocolon with severe bleeding of a branch of the middle colic artery. The pancreas was completely split into two parts, vertically, almost exactly through the center, with a gap of fully 2 inches. Because of the wide separation it was impossible to carry out an end-to-end union. Therefore, several deep mattress sutures were used to close the raw surfaces. The injury had cut the splenic vein, which was ligated. A large gauze was inserted and the wound was closed.

A pancreatic fistula developed but it closed after nine weeks. Pancreatic drainage decreased on a low protein diet and increased on an ordinary diet. The patient had lost considerable weight during the nine weeks that the pancreatic fistula was open. After closure of the fistula, the weight returned to normal in six weeks. The only final disability that remained was a small incisional hernia.

JOSEPH GASTER, M.D.

Morton, J.: Acute Pancreatitis. *Surgery*, 1945, 17: 475.

By means of Somogyi's rapid method of determining the blood amylase level, a determination can be made in twenty minutes. Eighty per cent of normal adults have an amylase level between 80 and 150, while levels below 60 and above 200 are considered abnormal.

There are two pathological types of acute pancreatitis—the more common acute pancreatic edema, called interstitial pancreatitis by Elman, and the type presenting hemorrhagic necrosis. The first subsides spontaneously if left alone; the second is a more serious condition.

The amylase test aids in establishing the diagnosis of acute pancreatitis. By studying the course in the hospital, acute pancreatic edema can be differentiated from hemorrhagic necrosis of the pancreas. The former usually gives a history of previous attacks, less prostration at the onset, and a high amylase reading. Over the course of three to five days the attack subsides spontaneously. Pancreatic necrosis, on the other hand, is almost always prostrating at the start; the amylase values may or may not be elevated; the patient fails to improve without surgical intervention.

The edematous type is treated conservatively during the attack, and later the gall bladder is removed, the common duct explored, and the sphincter of Oddi dilated. All cases of pancreatic necrosis demand operation as soon as the diagnosis is made and the patient is prepared. The necrotic tissue should be given a chance to extrude itself above or below the stomach, or through the epiploic foramen. If the common duct is blocked it should be drained.

After becoming familiar with the amylase test the author treated 29 cases of pancreatic edema conservatively without a death.

EARL O. LATIMER, M.D.

MISCELLANEOUS

Hughes, F., and Lambeth, S. S.: Pulmonary Complications following Appendectomy and Herniorrhaphy. *Surgery*, 1945, 17: 533.

Hughes and Lambeth report the pulmonary complications following 400 operations for hernia and 361 operations for appendicitis in the Station Hospital, Camp Rucker, Alabama. All followed lower abdominal operations on healthy young men between eighteen and forty years of age, done under spinal anesthesia (150 mgm. novocain) used routinely. The differentiation of atelectasis, bronchitis, pneumonitis, and bronchopneumonia was dependent upon clinical observation with roentgenographic studies.

There were 35 cases (4.6 per cent) of pulmonary complications, 22, or 5.5 per cent, after herniorrhaphy and 13, or 3.6 per cent, after appendectomy.

Of the complications following hernia operations, atelectasis alone or with pneumonitis was found in 12 instances, whereas bronchopneumonia or bron-

chitis was found in 10. Of the complications following appendicitis operations, atelectasis alone or with pneumonitis was found in 5 instances, bronchopneumonia or bronchitis in 7, and a lobular infarct was found in 1 case.

Spinal anesthesia was used routinely and there were 32 (4.8 per cent) complications after 671 spinal anesthesias and there were 2 (3.9 per cent) complications following 51 spinal anesthesias supplemented with general anesthesia. It is generally believed that the anesthetic is not a great factor in causing pulmonary complications or that spinal anesthesia will prevent pulmonary complications.

There was no mortality in the 761 cases.

The prevention of pulmonary complications is possible by attention to many details which influence and predispose to its occurrence. In one-third of the cases there was a history of respiratory infection, tooth infection, or sinusitis immediately prior to, or at the time of, operation. The eradication of infection in the nose, mouth, or respiratory tract and a lapse of from seven to fourteen days before operation is desirable. An acute phase of a chronic pulmonary infection in the presence of bronchiectasis should be allowed to subside completely. The pulmonary bronchial system, before, during, and after the operation, should be kept clear. For these lower abdominal cases the patient was asked to clear his bronchi prior to operation and a slight Trendelenburg position was used during the operation. The patients were usually ventilated at the end of the operation with carbon dioxide, and the importance of deep breathing, coughing, expectorating, and moving the legs was stressed. They were encouraged to cough, and were assisted in coughing. When bronchial secretion was obviously present and the patient was having difficulty expectorating, carbon dioxide and oxygen ventilation was given twice daily.

The psychological inhibition of coughing cannot be overemphasized. Coughing causes a pain in the wound and the patient thinks of tearing the repair with the development of another hernia, which is a real, tangible experience, whereas he probably has never heard of pulmonary complications. In the great majority of cases, this is easily overcome by explanation before operation, repeated during the operation by the anesthetist, and by frequent visits, reassurance, and personal contact postoperatively. Not the least of this reassurance is aiding the patient in coughing by holding his wound while he coughs and at times giving a few sharp slaps on the back. To reinforce this psychotherapy and actually stimulate deep breathing, carbon dioxide and oxygen inhalations have been used frequently for a few days.

Sulfadiazine and sodium bicarbonate are used routinely with pulmonary complications because of the frequent impossibility of differentiating infection from atelectasis early in the process, and because atelectasis is frequently found to be associated with infection.

Catheter aspiration or bronchoscopy is advocated if conservative measures fail.

STEPHEN A. ZIEMAN, M.D.

GYNECOLOGY

UTERUS

Hultberg, S.: Recurrence in Irradiated Carcinoma of the Uterine Cervix (Studien ueber Rezidive bei bestrahltem Carcinoma colli uteri). *Acta radiol.*, Stockh., 1944, 25: 59.

In order to judge the number of absolute cures obtained at the Radiological Clinic in Lund, only the material for which treatment was finished by the end of 1937 could be included in this study. This material consisted of 451 cases, and of these, 144 (31.4 per cent) were cured.

However, with regard to the problem of recurrence, more recent material could be utilized, since most recurrences take place within the first year following termination of the treatment. This recent material constituted a group of 535 patients treated up to the end of the year 1939. Primary healing had occurred in 281 and of these 281 patients, 90 later developed a recurrence, a total rate of 32 per cent. Twenty-five per cent of these recurrences were local, that is, they were confined to the portio, cervix, or fornices vaginae, when first detected. The author then attempted to determine whether these recurrences could be forestalled by hysterectomy, or removal of the involved area, after the cessation of the irradiation treatments. With the advice and encouragement of Professor Axel Westman, at this time director of the gynecological clinic at Lund, he attempted this method of preliminary irradiation by the Stockholm method and followed it by hysterectomy a few weeks later. Professor Westman laid down the guiding principle that only total extirpation of the uterus should be done, the Wertheim operation being reserved for those cases in which operable extrauterine metastases are discovered at operation.

Therefore, during the period from 1935 to 1939, inclusive, 15 women were operated upon by this combined method. To these might be added 1 patient who had undergone irradiation treatment in 1932, but had now returned for hysterectomy. At operation, gland metastases along the course of the great vessels were uncovered in 1 instance, and infiltration of cancer in the parametrial tissues on one side was found in 2 cases. Of the 8 patients operated upon by the Wertheim method, 3 developed fistulas; 1 a rectovaginal fistula of the diameter of a lead pencil, which caused her no trouble; another a vesicovaginal fistula which healed spontaneously after four months; and the third a rectovaginal fistula which healed a year after the establishment of a preternatural anus. There was 1 instance of fistula between the bladder and vagina among the cases not subjected to the Wertheim operation.

No trace of cancer was found in 9 of the 16 organs extirpated; in 5 there were what appeared to be vital cancer cells still present (in 4 of these cases the residual cancer was uncovered in the cervix, in the fifth the cancer cells were found in a parametrial gland), and in the remaining 2 specimens there was found what appeared to be a nonvital carcinoma damaged by irradiation. One patient who was operated upon early, three weeks after cessation of the radiation treatment, was completely cured, while another who was not operated upon until seven months after irradiation exhibited cells suggesting cancer of the cervix.

Of these 16 patients, 12 (75 per cent) are still free of symptoms from three to eight years after the operation. Of the 9 patients in whom carcinoma could not be demonstrated at operation, 8 are still alive and free of symptoms from four to eight years after hysterectomy; the ninth developed carcinoma of the vulva three and one-half years after operation. This tumor was electrocoagulated, and a half year later glandular metastases appeared in the inguinal region and progressed despite teleradium treatment; death occurred a half year later. Of the remaining 3 of the 12 patients still free of symptoms, 1 was free of symptoms for three years after the operation but then developed metastasis in the transverse colon, which could be extirpated. This patient is still living and is free of symptoms five months after the last surgical interference.

Of the 5 women who seemed to have vital residua of cancer in the extirpated cervix, 2 died one and one-half years later; the third developed a huge metastasis in the small pelvis and died from uremia before two years had elapsed; the fourth still lives free of symptoms four years after the operation, and the fifth, who at operation exhibited vital cancer in a parametrial gland although no cancer was found in the cervix, is still living five and one-half years after the extirpation and is free of symptoms.

The 2 patients whose cervices contained what seemed to be devitalized cancer cells damaged by irradiation are still living and free of symptoms, three and one-half and four and one-half years, respectively, following the extirpation of their uteri.

On the basis of the results of his investigations and consideration of the indications in the literature on this subject, the author believes that the method is worthy of trial, and recommends that in order to gain a better evaluation of the results, especially in younger women, this form of operation be practiced on a larger scale. JOHN W. BRENNAN, M.D.

ADNEXAL AND PERIUTERINE CONDITIONS

Millett, J., and Shell, J.: Meigs' Syndrome in a Case of Multilocular Pseudomucinous Cystadenoma of the Ovary. *Am. J. M. Sc.*, 1945, 209: 327.

In the last few years increasing attention has been given to the association of fibroma, or fibromyoma,

of the ovary with hydroperitoneum and hydrothorax, especially since the classical reports defining this condition were first published by Meigs and Cass in 1937, and by Meigs in 1939.

Reports concerning the association of benign ovarian tumors other than fibromas with ascites and hydrothorax are also beginning to appear. Vogt reported a case of granulosa-cell tumor of the ovary associated with hemoperitoneum and hemothorax. Traut and Marchetti, analyzing a group of 61 tumors of the granulosa-cell type, stated that in one of their cases hydrothorax was a prominent symptom and that abdominal fluid was found upon operation. McFee reported a case in which a multilocular cystadenoma of the left ovary, weighing 17 pounds, was associated with abdominal ascites and hydrothorax. Perlmutter observed this same syndrome, in which a thecoma of the right ovary was later found at operation. Kelemen recently reported a case due to a Brenner tumor of the ovary.

In addition, it has been found that benign tumors of the pelvic organs, other than those of ovarian origin, can give rise to the syndrome of abdominal ascites associated with pleural effusion.

The authors report a case of pseudomucinous multilocular cystadenoma of the ovary associated with hydroperitoneum and right hydrothorax. In common with all of the cases mentioned herein, and regardless of the origin, or of the cellular structure of the benign pelvic tumor, complete cure was obtained in this case.

A diagnosis of malignant neoplasm of the pelvis with metastasis to the right pleural cavity was made, and an exploratory operation was performed following removal of the chest fluid.

At laparotomy, a large ovarian cyst was delivered without difficulty. There was a moderate amount of yellow peritoneal fluid, and occasional mucinous implants were noted on the peritoneal surfaces. One peritoneal implant was removed for pathological examination. The postoperative course was uneventful.

Pathological report. A multilocular pseudomucinous cystadenoma of the ovary. Peritoneal implantation of tumor tissue.

Comment. The frequency of abdominal ascites by itself varies in these cases. A recent clinical and pathological study of 283 cases of ovarian fibromas by Dockerty and Masson, of the Mayo Clinic, revealed 3 cases of Meigs' syndrome. Inasmuch as inflammation, pedicle twists, and omental adhesions are infrequently found in association with the fluid, and inasmuch as the fluid disappears on removal of the tumors, one must agree with Meigs that there is cause and effect in this connection. At present, and until further experimental findings prove otherwise, abdominal fluid may be assumed to reach the pleural cavity by way of the lymphatics.

Clinically the patient presents a variety of symptoms and a few outstanding physical signs. She is anywhere between thirty-four and seventy-five years of age. She may or may not have had children. She may appear acutely, chronically, or gravely ill. Complaints referable to the chest are dyspnea, gradually increasing, either at rest or on moderate exertion. Orthopnea is a prominent symptom. Chest pain is rare, although a "heaviness" in the chest may be felt. Abdominal complaints are usually those of enlargement. There may be respiratory embarrassment.

The prognosis in Meigs' syndrome is excellent if the ovarian tumor is removed. The importance of this syndrome lies in the fact that it is a benign disease which is easily and permanently cured by laparotomy and removal of the offending tumor. The syndrome is fatal only when misdiagnosed, which places the responsibility of the outcome directly on the shoulders of the medical profession.

DANIEL G. MORTON, M.D.

MISCELLANEOUS

Marwil, T. B.: Functional Amenorrhea in Waves. *U. S. Nav. M. Bull.*, 1945, 44: 569.

The author analyzes 100 cases of functional amenorrhea which occurred at a naval training station among 5,000 Waves. These patients were given thorough physical examinations and no gross abnormalities were found. Because of this it was decided to study ovarian function. The methods used were the "single differential stain of Shorr" and the "vaginal glycogen index" of Mack. These tests were used to indicate the presence of normal ovarian activity or estrogenic deficiency.

The findings in this series of observations disclosed that all of these 100 Waves were in good health and were asymptomatic except for the amenorrhea. All had had normally occurring menses. These patients were observed for four months. Menses occurred in 30 following eight weeks of amenorrhea, in 33 following ten weeks of amenorrhea, in 30 following eleven weeks, and in the remaining 7 no menses occurred in the four-month period of observation.

When the tests for ovarian function were made, 83 per cent of these patients exhibited evidence of ovarian hypofunction.

The etiology of functional amenorrhea is discussed and it is suggested that psychic influences are important in the causation of this condition.

The therapy used in this group of patients was psychotherapy and 1 gr. of desiccated thyroid daily for one month.

HARRY FIELDS, M.D.

Horn, P., and Cowper, H. H.: Sodium Penicillin in the Treatment of Presumably Sulfonamide-Resistant Female Gonorrhea. *West. J. Surg.*, 1945, 53: 108.

Sodium penicillin has been advocated for use in sulfonamide-resistant gonorrhea in females. Excellent results have been reported with this form of treatment. In view of the variables influencing the course of gonorrhea and the variable extent of the pathological process, the authors felt that a different conclusion should be expected.

The following problems are considered in this report: (1) apparent bacteriological success in sulfonamide-resistant female gonorrhea attributable to penicillin therapy; (2) the extent of the pathological process in relation to drug response; and (3) the duration of the disease as it may affect the response to this drug.

Seventy-one females and 14 males were studied. All except 6 had failed to respond to two or more courses of sulfathiazole or sulfadiazine. Five had received one course of a sulfonamide. A course of sulfonamide is described as being between 20 and 48 gm.

All patients were hospitalized and followed up carefully with frequent cultures and examinations. A "positive" test for neisseria, after one or more courses of sulfonamide, was interpreted as sulfonamide-fastness. These drug failures were then considered candidates for penicillin therapy.

Penicillin was given intramuscularly in 4 c.c. of sterile distilled water or saline solution, according to schedules ranging from 20,000 to 50,000 Oxford units every three hours for a total dosage of from 100,000 to 200,000 Oxford units.

Seventy-four courses of penicillin were administered to 71 female patients who were presumed to have sulfonamide-resistant gonorrhea, and presumptive failures to penicillin resulted in 21.6 per cent.

It was noted that the failure rate for those women having lower genital-tract infection only was much lower than that of cases having associated upper genital-tract infection; 35.5 per cent of the latter cases failed to respond to penicillin. Also, the older the infection, the less the chance of success with penicillin therapy.

The authors infer from these results that early diagnosis and early institution of penicillin therapy are paramount considerations in the control of gonorrhea. In the female in whom diagnosis and cure are difficult to establish and time-consuming, delay caused by a preliminary trial with the sulfonamide drugs may diminish the possibility of cure.

HARRY FIELDS, M.D.

Sanders, J. T.: Factors Influencing the Morbidity and Mortality Rates in Gynecologic Surgery, Based on an Analysis of 500 Consecutive Cases in Private Practice. *South. M. J.*, 1945, 38: 209.

Five hundred consecutive recent gynecologic operations in private practice have been analyzed from the standpoint of morbidity and case fatality and have been compared with a similar series of 1,000 cases reported in 1935.

The second series shows a case fatality rate of 0.2 per cent, as compared with a gross fatality rate of 1.8 per cent and a corrected fatality rate of 0.9 per cent for the former series. It also shows a reduced incidence of major postoperative complications, although the criteria of selection were stricter in the second series than in the first.

Preoperative and postoperative care was basically the same in both series. In the second series, however, full advantage was taken of recent therapeutic improvements, particularly the more liberal use of intravenous fluids and of whole blood and plasma transfusions, and the earlier and more frequent use of intestinal decompression. To these improvements, as well as to more careful and more constant observation to detect complications in their incipiency, can be attributed the improved results in this second series.

The single death in the second series occurred in a woman twenty-six years of age, who died on the operating table under intravenous sodium pentothal anesthesia, which presumably was administered too rapidly. She was undergoing diagnostic curettage for metrorrhagia of undetermined origin.

EDWARD L. CORNELL, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Davey, J. F., and Daley, D. E.: A Critical Survey of 2 Diagnostic Pregnancy Tests. *Canad. M. Ass. J.*, 1945, 52: 371.

Although the number of pregnant women accepted for duty in the Royal Canadian Air Force is only between 5 and 8 per 1,000, their elimination at the time of the initial physical examination would be desirable. Because the expense involved in running routine Aschheim-Zondek or Friedman tests would be too great for the result obtained, the authors attempted to utilize the colostrum test and the histidine test on a specimen of urine to screen the pregnancies. A description of the procedure involved in the interpretation of the colostrum test and the analysis of the histidine test is included.

The colostrum was prepared according to the method originally described, and the injections were made and the results interpreted by one individual. Aschheim-Zondek or Friedman tests were run on all women showing a positive reaction or a pseudopositive reaction. Histidine tests were run on these same individuals, and on all a pelvic examination was made.

The results of the colostrum skin tests on 542 women are listed in Table I. The tests at the Women's College Hospital and at the Royal Candian Air Force examining center were carried out by the authors. Forty-three per cent of nonpregnant women gave either a definite pregnancy or a weak pregnancy reaction by this test.

The results of the histidine test are shown in Table II. Of 1,016 nonpregnant women, 12.4 per cent gave a positive pregnancy reaction, and in 8 definitely pregnant women a negative reaction was obtained in 6.

The authors are of the opinion that neither of these tests is specific enough, at least in their hands, to be utilized in detecting isolated cases of pregnancy

TABLE I.—RESULTS OF THE COLOSTRUM TEST

Reaction to colostrum intracutaneous test	1 University of Illinois College of Medicine		2 Women's College Hospital, Toronto		3 R.C.A.F. (W. D.)	
	Number[1]	Per cent	Number	Per cent	Number	Per cent
Known pregnant cases:						
Positive (pregnancy) reactions	260	98.1	24	63.2	1	14.3
Pseudo (weak pregnancy) reactions	3	1.1	8	21.0	3	42.9
Total positive (pregnancy) reactions	263	99.2	32	84.2	4	57.2
Negative reactions	2	0.8	6	15.8	3	42.8
	265	100.0	38	100.0	7	100.0
Known nonpregnant cases:						
Positive (pregnancy) reactions	7	2.2	0	0	58	10.8
Pseudo (weak pregnancy) reactions	3	1.0	6	23.1	172	32.2
Total positive (pregnancy) reactions	10	3.2	6	23.1	230	43.0
Negative reactions	303	96.8	20	76.9	305	57.0
	313	100.0	26	100.0	535	100.0
Total number tested	578		64		542	

[1]Does not include a group of 45 children in whom positive reactions were obtained up to about ten years of age and negative results thereafter.

TABLE II.—RESULTS OF THE HISTIDINE TEST

	Known pregnant cases		Known nonpregnant cases		Total
	No.	Per cent	No.	Per cent	
Positive (pregnancy)	1	12.5	34	3.3	35
Weak positive or doubtful	1	12.5	92	9.1	93
Total positive reactions	2	25.0	126	12.4	128
Negative	6	75.0	890	87.6	896
Total	8	100.0	1,016	100.0	1,024

among large groups of supposedly nonpregnant women. J. ROBERT WILLSON, M.D.

Bigby, M., and Jones, F. A.: Pregnancy and Diabetes. *Brit. M. J.*, 1945, 1: 360.

The adequate use of insulin has decreased the maternal mortality rate in the presence of diabetes, but the fetal death rate remains high. In 1942 Lawrence and Oakley had a maternal mortality of 2 per cent and a fetal death rate of 37 per cent, but when only their 40 completely supervised cases are considered the latter figure falls to 23 per cent. Bill and Posey (1944) give a 27 per cent fetal death rate.

In this series of 12 cases there were no maternal deaths, but 2 fetal deaths (17 per cent). The diabetic risks to the mother are ketosis and hypoglycemia, particularly in labor and the early puerperium; but with careful management they can be minimized.

Increased liability to toxemia is said to be the most important risk, and a high incidence is recorded by American writers. Herrick and Tillman (1938) reported toxemia in 18 per cent, and White and Hunt (1943) found the incidence as high as 42 per cent in 119 pregnancies. Lawrence and Oakley (1942) found toxemia in only 10 per cent of their 54 cases.

Diabetics tend to produce fat and postmature infants. Lawrence and Oakley (1942) think they reach maturity at about thirty-seven weeks, and that if they are not delivered until they are forty weeks old they are really postmature. The large size (up to 12 lb.) may be due to the excessive absorption of sugar or to the increased production of growth hormone by the pituitary gland. The second possibility is favored, as it does not seem possible to control the size of the baby by controlling the diabetes. The heaviest infant was born to the mother whose diabetes seemed well controlled by 130 units of insulin daily.

Premature death of the fetus in utero may occur, particularly if the pregnancy is allowed to continue to term, and Lawrence and Oakley mention that 7 of the babies of 19 patients who were left to go into labor spontaneously were stillborn. In this series 1 pregnancy miscarried at the twenty-third week, the fetus having been dead from two to three weeks, and 1 baby died in utero at the thirty-third week. The patient was in the hospital awaiting induction with the diabetes satisfactorily controlled when the child died.

Hydramnios is particularly liable to occur, and was present in 5 cases of this series. Neonatal death may occur from fetal hypoglycemia caused by overdevelopment of the pancreas in utero. Sugar was given prophylactically in this series and this complication was fortunately not encountered. Fetal abnormalities are said to be more frequent than usual, but none were found in these cases.

The patients were given from 220 to 300 gm. of carbohydrate in a diet supplying between 2,000 and 2,500 calories. It is important to maintain a high carbohydrate intake. At first they were given their usual insulin arrangement. As their insulin requirements increased, for preference they were given soluble insulin in the morning and a mixture of zinc protamine and soluble insulin in the evening. In very difficult cases it may be advisable to use a third injection of soluble insulin before lunch.

During labor the usual diet was given as long as possible, and then glucose (or lactose) from 15 to 20 gm. at two-hour intervals, and an extra 30 gm. at the onset of the second stage. The muscular effect of labor reduces the insulin requirements and there is real danger of hypoglycemia.

After delivery less insulin is needed as a rule, and a satisfactory working arrangement is to give half the usual amount on the following day and build up the dose if necessary.

Premature delivery at the thirty-sixth or seventh week is advisable because of the risk of fetal death in utero near term and because of mechanical difficulties due to overlarge babies.

Cesarean section has been widely advocated. In Lawrence and Oakley's series there were 27 cesarean sections with 2 stillborn babies and 2 neonatal deaths; 1 mother died from pulmonary embolism.

Premature delivery by the surgical induction of labor was advocated by Brandstrup and Okkels (1938), and its further trial was recommended by Lawrence and Oakley (1942), who had had satisfactory experiences in 3 patients. This method has been used in the present series, which includes 2 primigravidas. High rupture of the membranes with the Drew-Smythe catheter was performed, and pitocin (2.5 units hourly) may be given for 6 doses if necessary. Labor pains started without undue delay in all but 2 patients. Delivery was spontaneous in all but 1 patient, who needed a forceps delivery for fetal distress.

For the first twenty-four hours after birth the babies were given glucose (1 teaspoonful in ½ oz. of water every two hours) in an attempt to prevent hypoglycemia. This was given every three hours for the next day or two, and the infants were breast-fed or given expressed breast milk as soon as possible.

DANIEL G. MORTON, M.D.

Kobak, A. J., Fitzgerald, J. E., Freda, V. C., and Rudolph, L.: Carcinoma of the Cervix and Pregnancy. *Am. J. Obst.*, 1945, 49: 307.

Eight cases of carcinoma that appeared during a pregnancy were clinically studied in the past five years. The uneven distribution of these cases (6 were noted in one year), would render untenable a statistical evaluation of their incidence on the Cook County Hospital services. Many white and negro patients are seen annually, and it appears that carcinoma of the cervix, at least during pregnancy, might be more frequent in white women. In 7 patients the malignancy was a stratified squamous-cell carcinoma and in 1 patient, who died undelivered, it was an adenocarcinoma.

There is a tendency to regard carcinoma of the cervix during pregnancy as so improbable that other

causes of bleeding are given stubborn precedence in diagnosis and therapy. The malignancy is thus diagnosed more often toward the end of pregnancy, when the growth has achieved large proportions. Carcinoma of the cervix, contrary to the opinion of several contributors, continues to develop at a rapid pace during pregnancy. The earlier the diagnosis is established, the sooner effective therapy may be instituted, and the better is the ultimate prognosis.

The treatment of these cases depends upon the disposition of the pregnancy. In the first trimester the pregnancy is disregarded and deep x-ray therapy is instituted. With the death of the fetus, radium is added to the treatment. In advanced pregnancy, there is added concern for the cervix. It should be spared the injuries that occur during parturition. If there is no infection as noted by the temperature or character of the vaginal discharge, a classical cesarean section is performed to spare the cervix and to leave intact the fundal portion of the uterus to facilitate the radium therapy; this therapy is started after uterine involution has occurred. A total of 4,500 mgm. hours of radium is given in three equally divided doses. As soon after the delivery of the baby as possible, deep x-ray treatments are started, and continued for a long period of time. In the presence of local infection, as judged by the criteria mentioned, a Porro cesarean section is preferred. In pregnancies close to viability the cesarean section may be deferred, and from 1,500 to 3,000 mgm. hours of radium may be given to the cervix to inhibit the progress of the new growth temporarily.

The ultimate prognosis for the patient hinges on the persistent continuation of the deep x-ray and radium therapy that is instituted after the disposition of the pregnancy. The patient must be advised of the seriousness of her condition directly or indirectly. EDWARD L. CORNELL, M.D.

LABOR AND ITS COMPLICATIONS

Johnston, R. A.: A Critical Analysis of Twenty-Two Years' Experience with Cesarean Section. *Am. J. Obst.*, 1945, 49: 576.

The author performed 362 cesarean sections in a series of 5,975 term or near-term deliveries, an incidence of 6 per cent.

A brief history of the management of cesarean-section cases in Houston, Texas, is given with an analysis of twenty-two years' experience. The incidence of cesarean section in private practice limited to obstetrics was found to be 6 per cent. Reasons for this relatively high rate are given.

Morbidity and mortality figures obtained by obstetricians are compared with those obtained by well recognized general surgeons and by general practitioners. Nitrous-oxide-ether anesthesia was the anesthetic of choice, but maternal and fetal mortality rates for all types of anesthetics used are given.

The low cervical type of cesarean section outnumbered all other varieties performed in this series by 2.5 to 1. Pelvic dystocia was the primary indication for the procedure in the great majority of the 362 operations. Maternal and fetal mortality rates associated with each indication are tabulated. The survival rates are tabulated against the birth weights of the infants in the toxemia group, and it is concluded that one is hardly justified in performing cesarean section in the interest of the child if it weighs less than 3 pounds, but that there is a definite place for cesarean section in salvaging children from mothers with toxemia if the fetus weighs from 3 to 4 pounds or more.

The fetal mortality is also tabulated against the primary indications for cesarean section and important conclusions are drawn. The gross fetal mortality for the current series was found to be 4.4 per cent and the corrected rate, 1.4 per cent.

Brief summaries of the maternal deaths are recorded. The gross maternal mortality rate in this series was 2.2 per cent, while the corrected rate was 0.83 per cent. EDWARD L. CORNELL, M.D.

Ullery, J. C.: Delivery of Quadruplets by Cesarean Section. *J. Am. M. Ass.*, 1945, 128: 183.

The incidence of quadruplets varies in different countries as disclosed in the following statistical reports: Guzzoni in 1889 found them to occur once in 757,000 births; in 1895 Hellin of South Germany suggested the easily remembered ratios—twins once in 80 births, triplets once in 80 × 80 (6400) births, and quadruplets once in 80 × 80 × 80 (512,000) births; and Greulich in 1930 studied more than 120,000,000 births from 21 countries and found quadruplets to occur once in 670,734 births.

The following case is reported because a survey of the literature fails to reveal any previous quadruplets which were born by cesarean section.

The patient was a thirty-one-year-old white woman who had had a cesarean section two years before this admission for abruptio placentae. The baby was stillborn. Her postpartum course was stormy with a temperature elevated between 104 and 106 degrees for twelve days.

In the present pregnancy, the last menstrual period was March 12, 1944, with the expected date of confinement December 19, 1944. During the first four months of the antepartum period, she complained of considerable nausea and vomiting, so much so that in June she was hospitalized for one week for pernicious nausea. She responded well and was discharged improved.

In August the uterus was found to be larger than normal for the duration of pregnancy. X-rays at this time revealed the presence of four fetuses. The patient was immediately hospitalized and remained so until three weeks after delivery. During this time, her uterus enlarged rapidly, until near the termination of the pregnancy it was difficult for her to turn from side to side. She was given a high vitamin diet and progesterone (5 mgm. every other day) plus iron and extra vitamins.

On October 24 she began to have some irregular uterine contractions and the uterus became quite

tense. Because of the previous cesarean section and the stormy convalescence, it was believed that possible rupture of the uterus might be imminent and that any labor might precipitate this condition. Another cesarean section offered the safest procedure to avert it. Continuous, fractional, spinal anesthesia was chosen because of its low toxicity and high degree of safety to the infants.

A classical cesarean section was performed on November 1, 1944, and one placenta was found on the anterior wall, so that it was necessary to go through it to reach the infants. The first was delivered as a bilateral footling, the second also as a double footling, and the third was delivered in vertex presentation. These were all females and were enclosed in a single sac. The fourth was a male and was in a separate amnion with a small separate placenta.

The weights at birth were 3 pounds 14 ounces, 3 pounds 9 ounces, 3 pounds 1 ounce, and 2 pounds 14 ounces, respectively. The infants breathed and cried instantly on removal from the uterus and showed good muscle vigor.

At the end of six weeks, the respective weights were 4 pounds 15 ounces, 4 pounds 14 ounces, 4 pounds 6 ounces, and 4 pounds, respectively. Their feedings consisted of breast milk from a milk bank stationed at the hospital. The mother's convalescence was completely uneventful.

HARRY FIELDS, M.D.

Free, E. G.: Five Hundred Consecutive Cesarean Section Operations. *Am. J. Obst.*, 1945, 49: 401.

The maternal mortality in the first two series comprising 1,000 cases of cesarean section was 0.8 per cent and in the last 500 cases, 0.4 per cent, a 50 per cent decrease. For the total or 1,500 cases it was 0.66 per cent. Four of the deaths in the first 1,000 cases resulted from infection of genital origin. No deaths in the last group were attributed to puerperal sepsis, as attested by autopsy.

The morbidity in the earlier series was 43.8 per cent. The morbidity in the latter group was 31 per cent. This was a decrease of 29 per cent in total morbidity in the last four years. The combined morbidity for the entire 1,500 cases was 39.5 per cent.

Fetal mortality was noted to be 6.7 per cent in the first 1,000 cases. In this latter series, it rose to 9.2 per cent. Part of this rise in fetal mortality was due to a rise in the incidence of section in toxemias. In the first 1,000 cases, 12.3 per cent of the sections were performed with the indication of toxemia and related conditions. In the latter group 18.4 per cent of the sections were attributed to toxemia. The necessity for early interference in the fulminating toxemias increased the fetal mortality.

The incidence of section in the earlier group was 5.5 per cent, while the recent series showed a section incidence of 4.43 per cent, a decrease of approximately 20 per cent.

There was a variance in the relationship of indications for section between the first and latter series. The greatest disparity was noted in three groups. Multiple sections increased from 27.9 per cent in the first series to 38.8 per cent in the latter. More individuals who have had section are returning for reoperation. Cardiac pathology as an indication for section was noted as 10.4 per cent in the first 1,000 sections, but it was down to 3 per cent in the latter study. The incidence of cesarean section in heart disease is on the decrease for two reasons. Many of these cases in which pregnancy is a distinct hazard are being interrupted early with sterilization or with helpful contraceptive advice; and many others under careful medical observation and control are being carried to late viability, or term, with subsequent safe vaginal delivery.

Toxemia, as an indication for interference, accounted for 12.3 per cent of the sections in the earlier series; and for 18.4 per cent in the last 500 cases. This reflects the tendency to adopt an active obstetric attitude toward the problem of severe and unresponsive toxemia.

The low flap transperitoneal section is the operation of choice in the author's institution. The general procedure and technique have not changed, but critical attention as to indication and time for interference has contributed to improve statistics.

EDWARD L. CORNELL, M.D.

Hunt, A. B.: Massive Obstetric Hemorrhage Requiring Hysterectomy. *Am. J. Obst.*, 1945, 49: 246.

Accumulating evidence indicates that obstetric hemorrhage is now the most important and perhaps the most frequent cause of maternal mortality. Simple and well known conservative obstetric procedures can control the vast majority of obstetric hemorrhages if diagnosis is prompt and procrastination does not delay therapy. However, in a small group of cases (about 1 in 1,000) at the Mayo Clinic these simple measures were ineffective because of a pathological process in the fundus or the lower segment of the uterus. From July 3, 1935 to May 31, 1944, inclusive, there have been 5,620 deliveries at the Mayo Clinic and 8 patients have been treated by hysterectomy for hemorrhage.

The age of these patients varied from twenty-seven to forty-seven years, with an average age of thirty-four years. The parity ranged from 0 to 8, and averaged 2.

The cause of the extensive hemorrhage in the 8 cases was as follows: ruptured uterus in 4 cases; severe abruptio placenta in 2 cases; and intractable postpartum hemorrhage, associated with placenta previa and uterine fibromyoma, in 1 case each.

Six of the 8 patients had received prenatal care at the clinic. In general, the severe hemorrhages suffered by these patients could not have been prevented by prenatal care alone. These hemorrhages must properly be termed sudden, serious, "accidents of pregnancy." However, more vigilant and effective prenatal care might have averted 3 of the 4 fetal disasters and avoided such severe hemorrhages as to deprive 3 of the patients of their uteri.

There were 4 fetal deaths, or a mortality of 50 per cent. All of these deaths occurred prior to delivery, and in 3 cases the fetus was known to have expired before admission of the mother to the hospital. Rupture of the uterus was the cause of 3 fetal deaths and abruptio placenta accounted for the fourth death in this series.

Shock was present in each of these cases of severe hemorrhage, and in 5 it was profound. The volume of hemorrhage sustained by these women was large, and often tremendous. Large volumes of blood or blood substitutes, or both, were required to keep them out of dangerous shock and to carry them through the hysterectomy.

Cases such as these challenge the judgment and skill of the obstetrician and test his capacity to act quickly and effectively. Instances of such severe hemorrhage are rare in general obstetric practice. However, in the small group of cases in which such severe hemorrhages do occur, risk of death from exsanguination is exceedingly high. Laparotomy and repair or removal of the uterus is the first obstetric treatment to be applied for rupture of the uterus. For other types of intractable obstetric hemorrhages, laparotomy is, in a sense, a last resort, but it should not be delayed too long.

The purpose of this article is not to urge the frequent use of hysterectomy in the treatment of obstetric hemorrhage, but to point out its important place in the reduction of maternal mortality from exsanguinating hemorrhage when it is indicated. The operation is indicated when the uterus is the site of a lesion provocative of tremendous hemorrhage that is not accessible for hemostasis vaginally. Hysterectomy is indicated also when the usual methods of obstetric hemostasis, such as proper uterine tamponade through the vagina, fail. Once the indication has arisen, the operation should not be delayed, for in many instances such delay proves fatal.

Norton, J. F.: A Mortality Study of 187 Deaths in 66,376 Live Births. *Am. J. Obst.*, 1945, 49: 554.

One hundred and eighty-seven maternal deaths are presented from a maternity hospital having three paralleling services: (1) a clinic service which has, in close co-operation, antepartum, intrapartum, and postpartum services under the supervision of appointed obstetricians; (2) a nonclinic service offering hospital facilities for the emergent and oftentimes for the "in extremis" type of patient; and (3) a private service to which any ethical physician in the county may send his private patients.

Fifty-five of these 187 deaths occurring in 66,376 live births had sufficient clinical aspects to warrant their being labeled preventable as far as the hospital management of the case was concerned, a ratio of 0.82 per 1,000 live births.

No attempt was made to correct these 55, or to differentiate the nonclinic (emergency) or private cases from the clinic cases for which the hospital was fully responsible. No correction was made for postpartum readmissions, for home deliveries (except against puerperal infection), nor against the transfer of patients from other hospitals.

The "other toxemias" group presented a very difficult problem in assessing the preventability of maternal mortality. What good might have come from the prevention of pregnancy in this group the author was unable to say. Experience in dealing with it in reasonably far-advanced pregnancy was very unsatisfactory.

The greatest element of preventability in the entire group was in rupture of the uterus, hemorrhage, puerperal infection, eclampsia, and heart disease.

Rupture of the uterus, puerperal infection, and hemorrhage can be combated only by increased clinical vigilance and further improvements in general and special technique.

Some hope for a further reduction in rheumatic heart disease and the eclampsia groups is anticipated by earlier and longer periods of antepartum bed rest.

EDWARD L. CORNELL, M.D.

NEWBORN

Sanford, H. N., and Shmigelsky, I.: Purulent Parotitis in the Newborn. *J. Pediat.*, S. Louis, 1945, 26: 149.

Prior to this report, 57 cases of purulent parotitis in the newborn had been recorded. The authors report 5 additional cases observed during a period of five years in two hospitals following the delivery of approximately 10,000 infants during that period.

The organism cultured from the pus in every case in this report was the staphylococcus aureus hemolyticus, which is the predominating organism in the nasopharynx of infants from one to three weeks old, and is a potential pathogen. There were no constant etiological factors.

There was first an unexplained rise in temperature from 101 to 104° F., from the fourth to the twelfth day of life, commonly at about one week of age. Within twenty-four hours a swelling of the parotid gland was noted, accompanied by heat and redness. There was also anorexia and some loss of weight. The blood showed a marked leucocytosis (from 18,000 to 40,000), the leucocytes averaging from 65 to 80 per cent of the total white cells.

After the treatment, which is outlined, the gland rapidly increased in size and became fluctuant in three or four days. It then healed rapidly after incision, and recovery occurred in from one to two weeks. In about 35 to 50 per cent of the reported cases, other glands became infected during the course of from two to three weeks. These were the opposite parotid gland and various cervical glands; in all of these the primary organism was usually found.

As soon as the diagnosis was made by the presence of the swelling over the parotid, sulfathiazole was given by mouth, 2 gr. per pound in twenty-four hours in four doses. This was tolerated well and there were no reactions of any kind. As soon as fluctuation was observed in the gland, a small incision was made at the lower border, just over the

angle of the mandible. A probe was inserted and all pus pockets were evacuated. An iodoform gauze drain was inserted to keep the wound open for forty-eight hours, and a moist warm dressing was placed over the area. Healing was prompt, and there remained only a small scar that was imperceptible after a few months. The sulfathiazole was continued as long as there was any drainage, or until the leucocyte count had fallen markedly.

In all of the older literature, the prognosis was given as bad, particularly for smaller babies. The average mortality was given as 50 per cent, with no mortality in this series. ERNEST E. ARNHEIM, M.D.

MISCELLANEOUS

Guerrero, C. D.: Sterility; the Present Status of Its Study, and Methods of Diagnosis and Treatment (Esterilidad; estado actual de su estudio, medios de diagnostico y tratamiento). *Analecta med.*, Mex., 1944, 5: 1.

While sterility was formerly thought to be always due to some defect in the female, it is now known that it may be due to either male or female deficiencies, and an equally careful examination must be made of both partners.

The male examination should include an examination of the semen and the cells contained in it. It is not sufficient to say that there are many motile spermatozoa, any more than it would be sufficient in an examination of the blood to say that there are many red cells. Account must be taken of the vitality and motility of the spermatozoa, the presence of any abnormal forms, and the capacity of the semen for liquefaction. Spermatoculture should be carried out to exclude definitely any gonorrheal infection, and a biopsy specimen from the testicle should be examined. The basal metabolism should be determined in men as well as in women as it has been found that fertility is low in individuals with a low basal metabolism. The Huner test should be made, which consists of the microscopic examination of semen taken from the posterior cul-de-sac and endocervix from one and one-half to two hours after coitus.

In the woman a careful roentgen examination should be made of the whole genital tract to demonstrate any malformations that might interfere with penetration of the semen. The tubes may be occluded or the uterus retroverted. The Kurzrok-Miller test should be made to determine whether the endocervical secretion is permeable by the semen. A drop of this secretion and a drop of semen are placed on a microscope slide at a distance of about 3 mm. from each other; normally the semen will move toward the endocervical secretion and mix with it. A biopsy specimen of the endometrium should be examined and the amount of the various female hormones determined. The desquamation from the vagina should be examined and the vaginal *p*H determined.

The author reports the examination of 438 sterile patients from August 1, 1943 to July 31, 1944 at the Spanish Hospital of Mexico. He found that 31 per cent of the cases of sterility were due to abnormalities of the tubes, 29.1 per cent to abnormalities in the male, 16 per cent to hormonal factors, 11 per cent to conditions in the cervix, 2.8 per cent to retroversion of the uterus, and 10 per cent to various other causes. These statistics are very similar to those of investigators in other countries.

The author succeeded in bringing about pregnancy in 44 cases (10 per cent), but in only 3 of these cases was this result obtained by surgery. In 2 cases it was accomplished by a plastic operation on the tubes and in 1 case by myomectomy. The ideal treatment for sterility is therefore not surgical, and the practice of surgery in this condition has been much abused. The author urges that special centers be established for the study of sterility and that free clinics be established for the indigent classes.

AUDREY G. MORGAN, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

Flocks, R. H.: The Preventive Treatment of Calcium Urolithiasis; The Important Role of Early and Frequent Roentgenographic Examinations. *J. Urol.*, Balt., 1945, 53: 427.

Flocks, analyzing 51 cases of calcium urolithiasis following fracture of the spine, fracture of the pelvis, and traumatic stricture of the urethra, stresses the importance of frequent and early x-ray check-up examinations whenever conditions predisposing to calcium urolithiasis are or have been present. A tabulation of conditions predisposing to stone formation is given. Most important of these, according to Flocks, are hypercalcinuria, urinary stasis, and urinary-tract infection. When recumbency is necessary, hypercalcinuria cannot be prevented. For these cases an outline of treatment is presented:

1. The maintenance of a large fluid output
2. Control of the diet—a high vitamin A and B acid ash diet is desirable
3. Control of stasis by movement of the patient, catheter drainage, etc.
4. Control of infection
5. Continuation of treatment for three months after immobilization
6. Frequent roentgenographic examinations during the illness and for one year after immobilization.

WILLIAM W. SCOTT, M.D.

Bothe, A. E.: The Relationship of Epithelial Buds to Carcinoma of the Pelvis of the Kidney, Ureter, and Bladder. *J. Urol.*, Balt., 1945, 53: 451.

This study consists primarily of a microscopic search for cell nests in the ureters from 54 consecutive autopsies and in 12 surgical specimens of the urinary tract including 4 papillary carcinomas of the renal pelvis, 7 of the ureter, and 1 of the bladder. Epithelial cell nests were found in 38 of the 54 autopsy cases, but in no case was any neoplastic change found in association with urinary-tract buds or cell nests. In the surgical specimens, tissues distant and adjacent to the primary carcinoma were studied. These areas did not appear malignant or pathological, but microscopically they revealed subcutaneous hyperemia with round-cell infiltration and some digitation of the epithelial cells into the supporting tissue. Buds and cell nests were identical with those seen in the autopsy tissue.

Upon the assumption that there may be a relationship between epithelial buds and carcinoma, roentgen therapy was tried in 4 cases of urinary-tract cancer in an attempt to render these buds inactive or unsusceptible. In 2 cases of bladder papilloma treated by roentgen therapy and transurethral desiccation, recurrences have not been found. In 2 treated by transurethral desiccation alone recurrences have been observed. WILLIAM W. SCOTT, M.D.

Ingersoll, F. M., and Meigs, J. V.: The Treatment of Ureters Injured during Gynecologic Operations. *N. England J. M.*, 1945, 232: 335.

Accidental injury of a ureter is the most frequent serious complication of gynecologic pelvic operations. Seven ureteral injuries occurred in 590 total hysterectomies and 1 ureteral injury occurred in 170 supravaginal hysterectomies during a five-year period at the Massachusetts General Hospital, Boston. These 8 cases served to illustrate the type of injuries that occur and the surgical principles and procedures to be followed in repairing them.

Although each patient must be treated according to the circumstances in her case, there are certain important principles that should be observed when dealing with the problem of the damaged ureter. First, the immediate recognition of the injury is of the utmost importance. This is true especially since proper treatment at the time of operation may result in a successful anastomosis, with hospitalization no longer than that required for the routine uncomplicated procedure. In the 8 cases reviewed, injury was noted at the time of operation in 4. Three of these patients did well; the fourth developed a urinary fistula and a pelvic abscess, and later came to nephrectomy. Secondly, every effort should be made to preserve the kidney function on the side of the injured ureter until the function of the other side can be determined. Palpation is not an adequate means of determining renal function, and the sacrifice of a kidney by ligation or nephrectomy without knowledge of the status of the remaining kidney is unwise. Preservation of the kidney may be accomplished by nephrostomy, skin ureterostomy, or transplantation of the ureter into the bowel or bladder. The third important principle is that all ureteral anastomosis should be done over an indwelling nylon or rubber ureteral catheter. The catheter serves as a splint during the healing of the ureter and also acts to decompress the kidney pelvis, preventing distention at the site of the anastomosis. The indwelling catheter has proved itself to be the most vital single factor in successful anastomosis. It should remain in place for seven or eight days after operation. HARRY W. FINK, M.D.

BLADDER, URETHRA, AND PENIS

Van Duzen, R. E.: Operations for Urinary Control of Neurogenic Bladders. *J. Urol.*, Balt., 1945, 53: 565.

The nerve supply of the bladder comes chiefly from two sources. The sympathetic nerves reach the bladder chiefly by way of the presacral nerves, but some fibers pass by way of the sacral nerves. Stimulation of the sympathetic nerves causes contraction of the trigone muscle. The parasympathetic nerves reach the bladder through the sacral nerves and

supply the detrusor muscle of the bladder and the involuntary muscles of the bladder neck. Stimulation of the sacral nerves causes contraction of the bladder wall and of the "so-called" internal sphincter of the urethra. Section of the sacral nerves produces relaxation of the bladder and posterior urethra except when the prostate has enlarged and replaced the internal sphincter. In such cases, the section of the nerves may not influence the deep urethra because it may have become a rigid structure. The external or voluntary sphincter receives its nerve supply through the pudic nerves. Section of these nerves produces, in most cases, the true incontinence of the bladder without paralysis of the bladder wall. Lastly, we must consider injuries to the brain and upper spinal cord. These usually produce incontinence of the bladder.

Neurogenic bladder is often associated with like pathological changes in the rectum, and this immediately precludes the transplantation of the ureters into the rectum. Rose suggested converting the partially incontinent bladder into one totally incontinent. He deliberately made several cuts with the resectoscope through the external urethral sphincter. The urine was then controlled by the incontinence clamp. In selected cases, this is an excellent solution of a difficult situation.

The author uses the classification given by McLellan in "The Neurogenic Bladder": (1) the uninhibited neurogenic bladder; (2) the reflex neurogenic bladder; (3) the autonomous neurogenic bladder; and (4) the atonic neurogenic bladder.

The enuretic child is the best example of the uninhibited neurogenic bladder. Its counterpart is the overinhibited bladder of dementia praecox. The author has found many cases of enuresis improved by ephedrine. Ephedrine is a stimulant of the sympathetic nerves.

Ephedrine also acts upon the brain, and the author believes it may increase the inhibition that these cases lack. In a few cases treatment could not be continued because of extreme nervousness. Recently, the author used methyl testesterone with good results, but he has seen a few cases which did not respond to any medical treatment. He has resected the presacral nerve with excellent results in these cases.

The treatment of the remaining types of neurogenic bladder depends on whether the micturition is precipitate or involuntary. It it is precipitate, trasentin may be useful.

It has been the author's practice, in all cases of incontinence, to attempt to substitute a voluntary control for the lost sphincteric action. Lowslev's suggestion that ribbon gut be passed around the urethra has been unsuccessful in the author's hands because it produced a fibrous stricture which could not be relaxed voluntarily. In 1926, Deming reported the use of the gracilis-muscle transplant for the treatment of incontinence due to epispadias. Looney and the author modified Deming's operation by tunneling beneath the bulbocavernosus muscle rather than by cutting across it and they have preferred this operation. However, a successful result depends on the patient's walking with the leg slightly adducted. When the leg is abducted, the urethra is opened and urine escapes. For sleeping, some patients have used a "hobblelike" bandage at the knees to prevent abduction. Some patients have a flaccid knee joint and find it impossible to keep the leg adducted. Others have ulcers about the perineum or thighs from constant soiling, pressure from braces, or trophic ulcers. These cases are unsuitable for the gracilis-muscle transplant.

JOHN A. LOEF, M.D.

Cox, H. T.: Decompression for Chronic Prostatic Retention Controlled By Intravesical Pressure. *Lancet*, Lond., 1945, 248: 366.

Cox believes that decompression of the urinary bladder for chronic prostatic retention should be controlled by a record of the intravesical pressure during the period of decompression rather than by routine catheter decompression without pressure recordings.

He thinks that for the most part, cases can be divided into two groups. In group 1 the symptoms are predominantly urinary and in group 2 the clinical features are more general than local with loss of appetite and weight, vomiting, etc. Nine case histories were confined primarily to group 1. For this group it is recommended that retention is best treated by rather rapid decompression, the withdrawals of urine being regulated so as to reduce the intravesical pressure by approximately 10 c.c. per hour. Flexibility of the decompression based on the intravesical pressure changes rather than on the volume of urine withdrawn is strongly urged.

WILLIAM W. SCOTT, M.D.

GENITAL ORGANS

Crane, J. J., and Rosenbloom, D.: The Treatment of Carcinoma of Prostate Gland. *J. Urol.*, Balt., 1945, 53: 411.

In an attempt to evaluate the different methods of treatment of prostatic carcinoma, a study was made of 340 cases of prostatic cancer treated at the Los Angeles County General Hospital, Los Angeles, California, from July 1, 1938 to January 1, 1944. In addition to these cases there were included, as controls, 43 patients with prostatic cancer who did not receive any form of treatment. The method of handling the statistics (median values) is that given in Dahlberg's Statistical Method for Medical and Biological Students (London: George Allen and Unwin, Ltd., 1940. p. 65). The results, as indicated in Table I, were adjudged in the light of maximum survival time and maximum subjective improvement.

It is admitted that these statistics are not based upon an exhaustive material, and the authors do not claim to "cure" prostatic carcinoma by resection-endocrine therapy. Nevertheless, they are able to cite a number of cases in which a discouraged, suf-

TABLE I.—RESULTS OF TREATMENT OF PROSTATIC CARCINOMA

Treatment	Median survival time (From date of diagnosis)	Condition in one month	Condition in one year (And number of available cases)
None, 43 cases	*mo.* 1.78	No change 59% Worse 21% Dead 10%	No change 77% Better 11% Worse 11% (9 cases)
Surgical drainage (cystostomy or simple prostatectomy), 39 cases	5.39	No change 80% Better 11% Worse 11%	Better 52% Worse 24% No change 19% (11 cases)
Estrogens only, 16 cases	5.55	No change 54% Better 18% Dead 18% Worse 6%	Better 66% No change 33% (6 cases)
Estrogen and castration, 17 cases	5.6	No change 60% Better 35% Dead 5%	Better 75% Worse 25% (8 cases)
Transurethral resection only, 107 cases	5.94	No change 75% Better 20% Worse 5% Dead 1%	Better 42% Worse 30% No change 28% (36 cases)
Transurethral resection and estrogen, 24 cases	6.25	No change 53% Better 46%	Better 56% No change 35% Worse 7% (14 cases)
Surgical castration only, 7 cases	6.7	No change 56% Dead 28% Better 14%	Better 66% No change 33% (3 cases)
Transurethral resection and castration, 39 cases	8.5	*Better 54% No change 36% Dead 8% Worse 2½%	Better 55% No change 27% Worse 20% (14 cases)
Transurethral resection, castration, and estrogen, 39 cases	10.31	Better 55% No change 43% Worse 2% Dead 2%	Better 70% No change 27% Worse 5% (21 cases)
Radical perineal prostatectomy, 4 cases	12.0	Better 50% No change 50%	No change 100% (2 cases)

*Note that early subjective improvement occurred in a majority of these two groups only.

fering and bedridden patient was converted into an ambulatory individual who became self-supporting and showed a weight gain of from 25 to 40 pounds within a period of from six to nine months. In this regard they cite the example of a sixty-four-year-old male with a history of fever, weakness, and a weight loss of 50 pounds, who was found to have a hard, irregular, fixed, enlarged prostate, and multiple, enlarged, firm inguinal lymph nodes (adenocarcinoma of grade 2 on biopsy), and residual urine of from 500 to 600 c.c. A transurethral resection and subtunical orchectomy were done (the prostatic tissue was reported as adenocarcinoma grade 3), and thereafter the patient received 1 mgm. doses of stilbestrol orally. Eight days later, the serum acid phosphatase had fallen from 55 to 3.3. Eleven months later he showed a gain in weight of 45 pounds. At this time the patient was still taking stilbestrol and was working eight hours a day. Examination then revealed a flat prostate with only a suggestion of carcinoma.

From the data given and the clinical impressions of the authors, it is concluded that a patient with prostatic cancer should be given the advantage of combined therapy without hesitation.

JOHN W. BRENNAN, M.D.

McCrea, L. E.: The End-Results of Prostatectomy; A Five Year Survey. *J. Urol.*, Balt., 1945, 53: 466.

The end-results of prostatectomy as shown by this survey are startling. In this series of 367 individuals, 307 were ward and 60 were private cases. Four of the private cases terminated fatally within the five-year period following discharge from the hospital. Three of the recorded postoperative deaths were among the private cases. Fifty-five ward cases terminated in postoperative death. Five of the 139 individuals to whom inquiries were sent died within the five-year period of this survey. Of the 66 individuals who answered the questionnaire, 61 were well within the survey period.

A total of 114 (31 per cent) of the 367 patients who were subjected to operation are alive and well by their own admission. Undoubtedly many of the inquiries were not answered by individuals who are alive or well.

The most common surgical procedure was the suprapubic enucleation, which was done in 217 operations.

Postoperative hospitalization was thirty-two and six-tenths days in the city hospital, and twenty-seven and one-half days in the private hospital, with suprapubic drainage. This period of hospitalization was reduced to an average of seventeen and one tenth days when sump drainage was used.

The most frequent causes of death were cardiac failure (32 cases), pyelonephritis (9 cases), and bronchopneumonia (6 cases). JOHN A. LOEF, M.D.

MISCELLANEOUS

Jones, T. R. L., Maitland, F. G., Allen, S. J., and Dudley, S.: Penicillin in Gonorrhea; A Suggested Scheme of Treatment. *Lancet*, Lond., 1945, 248: 368.

A plan for penicillin treatment of gonorrhea used successfully in more than 99 per cent of 256 consecutive cases is described. Urethral cultures and smears were used for diagnosis and as criteria of cure. Penicillin blood levels were determined as an aid in determining the time-dose relationships. Treatment does not require hospitalization and is complete in eight hours. Deep intramuscular injections of 30,000 units of penicillin in 1.5 c.c. of water are given every two hours until five doses, a total of 150,000 units, have been given. Among the 256 cases treated there has been only 1 relapse. Of the first 200 cases, 26 were sulfonamide-resistant and 6 were receiving concurrent arsenicals and bismuth for the treatment of syphilis. Primary chancres developed in 4 cases treated for gonorrhea by penicillin, 2 at four weeks, and 1 chancre each at three and seven weeks, respectively, after exposure and penicillin treatment. This treatment schedule has been officially adopted for the penicillin therapy of gonorrhea occurring in the personnel of the British Navy.

WILLIAM W. SCOTT, M.D.

Platou, R. V., Hill, A. J., Ingraham, N. R., Goodwin, M. S., and Others. Penicillin in the Treatment of Infantile Congenital Syphilis. *J. Am. M. Ass.*, 1945, 127: 582.

This is a brief preliminary note concerning 69 infants with manifest early congenital syphilis who were treated with sodium penicillin. Penicillin was administered intramuscularly in saline solution every three hours in sixty injections over a period of seven and one-half days. The total dosages used ranged from 16,000 to 32,000 Oxford units per kilogram of body weight, with no other antisyphilitic treatment.

In general, the immediate response of early congenital syphilis to penicillin has been gratifying. Cutaneous and mucous-membrane lesions have healed during or shortly after treatment; rhinitis has been somewhat more persistent, healing in from two weeks to two months. All dark-field positive lesions became negative within twenty-four hours after the start of penicillin therapy. Roentgenographic evidence of osteitis disappeared in from two to six months, i.e., at about the same rate expected after metal chemotherapy. Regression of hepatic, splenic, and lymph-node enlargement, though variable, was usually complete by three months. If abnormal spinal-fluid findings were present initially, these returned to normal in all cases in from eight days to six months.

The results so far obtained in infants indicate that the present total dose and time-dose relationship schedule is not entirely satisfactory.

JOHN A. LOEF, M.D.

Anderson, K., DeMonbreun, W. A., and Goodpasture, E. W.: An Experimental Investigation of the Etiology and Immunology of Granuloma Inguinale. *Am. J. Syph.*, 1945, 29: 165.

The authors summarize the results of their experiments as follows:

1. A micro-organism morphologically identical with the Donovan body of granuloma inguinale and its unencapsulated bacillary forms was isolated and serially cultivated in the yolk of developing chick embryos.

2. The same micro-organism was isolated from the lesions of 3 patients with granuloma inguinale.

3. The Donovan micro-organism has not been amenable to cultivation on ordinary artificial culture media, on the chorioallantois of chick embryos, nor in the yolk of infertile eggs, and it is not pathogenic for mice, dogs, macaca rhesus monkeys, rabbits, or chickens.

4. Embryonic yolk in vitro supports the growth of the micro-organism.

5. Washed bacterial bodies stimulate an apparently specific cutaneous reaction in the skin of patients with active granuloma inguinale.

6. A "capsular" substance soluble in N/100 sodium hydroxide is precipitable from infected yolk with N/100 hydrochloric acid.

7. This "capsular" substance gives an apparently specific precipitation reaction in the patient's serum. It fixes complement in the patient's serum and stimulates a mild skin reaction in the skin of patients with granuloma inguinale.

8. In the authors' opinion, these experiments describe a culture medium suitable for the growth of the Donovan body which has hitherto not been cultivated outside of the body of the human host. They determine what seems to be the bacterial nature of the etiological agent of granuloma inguinale, and afford an avenue of approach to the solution of the isolation of its obligate growth factor, and the refinement of useful aids to diagnosis.

JOHN A. LOEF, M.D.

Shorr, E.: The Possible Usefulness of Estrogens and Aluminum-Hydroxide Gels in the Management of Renal Stone. *J. Urol.*, Balt., 1945, 53: 507.

Shorr presents the rationale for the use of estrogens and aluminum-hydroxide gels (amphojel) in the

treatment of nephrolithiasis in which the stone is composed of calcium phosphate or carbonate, magnesium phosphate, magnesium-ammonium phosphate, or calcium-magnesium-ammonium phosphate.

The author presents data to show that natural estrogens, by increasing the urinary citrate excretion, reduce the concentration of calcium ions taking part in the precipitation of calcium phosphate, and replace them with a weakly ionized soluble calcium-citrate complex. The same effect cannot be obtained by the oral administration of sodium citrate because the resulting increase in urinary citrate is almost entirely due to the elevation of the urinary *p*H by the sodium ion. The gain in urinary citrate is offset by the reduced solubility of the calcium phosphate in the alkaline *p*H range and by an increase in the urinary excretion of calcium. The estrogenic hormones increase the urinary citric acid without altering the *p*H, and generally with a reduction in urinary calcium excretion.

Aluminum-hydroxide gels, by diverting the phosphate excretion from the urinary to the intestinal tract, reduce the number of available phosphate ions participating in the reaction with calcium. Data are presented showing the relationship between the urinary excretion of phosphorus, calcium, and citric acid, and amphojel dosage.

Men given estrogen for the purpose outlined showed some reduction in libido and increased sensitivity of the nipples; women at times showed excessive endometrial hyperplasia and profuse withdrawal bleeding.

In the author's conclusion he states: "—too brief a clinical trial has been made to permit conclusions as to the actual effectiveness of these measures in the prevention of recurrence or of further stone growth." This preliminary report was presented to stimulate research on the subject.

WILLIAM W. SCOTT, M.D.

Werner, A. A.: The Male Climacteric. *J. Am. M. Ass.*, 1945, 127: 705.

This report represents a study of 54 male patients, each of whom had one of the types of testicular hypofunction or afunction, which is, or can be, the etiological factor in producing the hypogonadal or climacteric syndrome. With the exception of menstruation in the female, it is the same for the two sexes.

The symptoms have been discussed, so that the syndrome may be easily recognized.

Testosterone propionate, given by intramuscular injection of 25 mgm. three times a week, has been found effective in relieving the symptoms and in the production of a sense of well-being in the patients, which is the primary objective of this treatment. This medication should be administered for a period of two or three months. The patient may feel very well within a few weeks, but it is best to continue beyond this time for the purpose of stabilization. Testosterone may also be given orally, by inunction, and by implantation. The effective oral dosage is three to eight times greater than the intramuscular injection. Inunction of testosterone is not so satisfactory. Implantation allows no control of dosage.

Testosterone should not be given for the purpose of stimulating potency. While it occurs in some patients, this result cannot be promised and it is perhaps better for older men if this phase of the reaction does not result.

It is important that the duration of the climacteric be stressed, since it varies in different individuals. Some pass through it without much appreciable difficulty; some may have trouble for from three to six months, and in others the period for permanent endocrine equilibrium to occur may vary from one to four or five years. The latter group will need intermittent treatment for periods of from one to three months when aggravating symptoms recur.

JOHN A. LOEF, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Cole, W. H.: The Clinical Diagnosis, Treatment, and Prognosis of Epiphyseal Disturbances in Childhood. *J. Am. M. Ass.*, 1945, 127: 318.

The etiology of epiphyseal lesions is not clearly understood, and it is impossible with our present knowledge to classify these disturbances except on an anatomic basis. The name osteochondrosis has been applied, in the Standard Nomenclature of Disease, to most of the conditions involving growth centers of which the etiology is obscure or at least of which no unified opinion as to their cause exists, and our older and more familiar terms must be sidetracked for purposes of classification and filing if not for other reasons.

The epiphyses throughout the body have, of course, a very regular and constant anatomic position, and their ossification is also constant for any particular location. Some, a very few, show centers already present at birth, while others may remain completely cartilaginous until puberty, and it is an understanding of these different periods of development which forms a basis for the recognition of any pathological condition which may supervene.

In Legg-Perthes disease some cases certainly are never seen by a doctor, and some may present such minor symptoms that, when in later life a deformed hip is found because of developing disability, no history of earlier trouble can be obtained. It is this insidiousness of onset which is largely responsible for the delay in proper treatment in many cases, and not neglect on the part of the parents or the physician.

Eighty-five per cent of all patients are males. They are seen as young as three years of age and up into the teens, although an onset after twelve years is very rare. The first symptom in a typical case is usually a limp which develops as the day goes on but is absent after rest and on first getting up in the morning. Examination shows, even early in the disease, that there is limitation of the rotations, especially internally, and of abduction. The roentgenogram will be the final evidence needed to insure the diagnosis.

The first requirement of therapy is that weight bearing be discontinued. As it is impossible to keep all children with this lesion in bed for the length of time needed to allow healing to take place, some substitutes must be found for the ideal. The ring-caliper splint has been found to be satisfactory in this regard, and weight bearing through the hip can certainly be cut to a minimum if the splint is well fitted. In the more acute cases the brace, instead of being fastened to a ferrule in the shoe, is extended to a foot piece or patten below the shoe, with the shoe on the normal side built up to equalize the length of the two sides. Complete fixation of a hip joint in plaster-of-Paris is never indicated, unless for purposes of transportation.

The general treatment should consist of those measures necessary to keep the child in good health, and the use of the thyroid gland. It has been claimed that with early recognition of this condition, adequate thyroid therapy will eliminate the necessity for protective treatment, but even if thyroid will hurry the healing process, and the author's "limited" experience makes him feel that it does, it is certain that avoidance of weight bearing is essential also until the bone is firm enough to assume its full function. There can be little doubt that a practically normal hip will result if the case has been seen early and proper protection has been used. Those who show flattening and broadening of the capital epiphysis at the first examination will probably always have some distortion of the hip and a disability which, although negligible or absent at first, will become greater as the age increases. Even with the apparently perfect recoveries there will be a tendency toward the development of a degenerative arthritis in later life.

Slipping of the proximal femoral epiphysis occurs about twice as often in boys as in girls, and in close to 70 per cent of the cases the general body build is that which is frequently described as the Froehlich type of individual. The smaller percentage of patients are apparently physically normal children or the tall and thin, rapidly growing type.

Examination shows the extremity in some external rotation with a definite limitation of internal rotation and abduction. When the thigh is flexed on the trunk, it tends to go into external rotation and abduction, but hyperextension may be even freer than on the normal side. In later cases there will be some shortening of the extremity, with elevation of the trochanter above Nelaton's line. All of these symptoms and clinical findings are due to a gradual slipping and rotation of the femoral head downward and backward on the neck.

The lateral roentgenogram is absolutely essential if mistakes are not to be made.

The prognosis for a normal or near normal hip is good only if the case is seen and diagnosed in the early stages with no delay in instituting proper treatment. Older cases all show some disability, sometimes of a pronounced degree.

Treatment, in addition to the use of thyroid or other endocrine product, is aimed at correction of the deformity and the prevention of further slipping after this has been accomplished. The author has become therapeutically more and more conservative in the treatment of these cases. In cases in which approximate reduction is obtained by skeletal traction, and this may take several weeks, or in very early cases in which the slipping is as yet minimal, either lighter traction must be maintained until the epiphyseal line closes, or fixation of the head must be

assured by operative means. Multiple drilling, sliver bone grafts through drill holes, a large bone graft, the Smith-Petersen nail, and vitallium screws have all been used for this purpose and each has its advocates. There is probably not much choice between them, but it should never be forgotten that the operation, of whatever type, is only a means to an end, and that end is union of the epiphysis to the neck. Until this has taken place, recurrent slipping may happen at any time.

If reduction cannot be obtained by traction, one must decide to manipulate the hip, perform a radical operation immediately, or wait until fusion of the epiphysis has occurred in the deformed position and then resort to some type of osteotomy. The author has seen some excellent results from manipulation but many more poor ones, with stiffness amounting almost to ankylosis, and, not infrequently, aseptic necrosis of the head. The same is true of open reduction of the head and of wedge osteotomy of the neck, and he is therefore inclined to postpone radical treatment in these cases until a trochanteric osteotomy can be performed. In the meantime, progression of the lesion must be stopped by recumbency, with or without traction, or by the use of an efficient ring-caliper splint. The osteotomy will, at least partially, correct the deformity and will obviate the danger of further intra-articular pathological change.

Disturbances of the epiphyses other than at the hip, which come under the classification of osteochondrosis, are of relative unimportance once the diagnosis has been made, but great care should always be taken to rule out more severe conditions.

Vertebral epiphysitis does not occur until puberty, as the epiphyseal plates of the vertebral bodies develop at that time. Most cases are seen in boys between fourteen and seventeen years of age and the smaller group in girls somewhat earlier. The lack of acute symptoms and the rounded curve are the distinguishing differences from tuberculosis of the spine. The roentgenogram makes the diagnosis clear. With no treatment the rounding of the spine may increase, but in the end this deformity is the only symptom, and as the spinal epiphyses may not unite to the bodies until early in the twenties there can be progression up to this time. If seen and recognized early, part of the deformity, at least, can be prevented, and the symptoms alleviated by recumbency, plaster-of-Paris or brace support, and active muscular exercise tending to strengthen and straighten the back.

Osteochondrosis of the tuberosity of the tibia (Osgood-Schlatter disease) is a fairly common condition seen usually in active adolescent boys, which fortunately leads to no permanent disability. Treatment aims to relieve the symptoms by rest and lessening of the pull on the patellar tendon; thyroid may also be given. Many cases are overtreated.

Apophysitis of the os calcis is treated by reducing the pull on the Achilles tendon and by raising the heel; in acute cases a short period of complete rest may be required at first. Healing always takes place and there is never any residual disability.

Koehler's disease of Freiberg's infraction may require rest and protection to relieve the symptoms quickly, and no disability results after the epiphysis has united. A full length steel in the sole of the shoe or an anterior arch bar usually is sufficient treatment. The lesion in the tarsal navicular bone to which Koehler's name is given, although similar with regard to pathologic change, treatment, and prognosis, is not, of course, in an epiphysis.

ROBERT P. MONTGOMERY, M.D.

Doub, H. P.: Aseptic Necrosis of the Epiphyses and Short Bones. *J. Am. M. Ass.*, 1945, 127: 311.

Areas of necrosis involving the epiphyses and also the primary centers of ossification in certain of the short bones have been described by different observers. Unfortunately, in most instances the lesion has come to be known by the name of the original observer. This has the disadvantage of giving no hint as to the underlying pathological process and, further, of implying that in each instance we are dealing with an independent disease which bears no relation to the others in the series. These diseases have been known also under more general headings such as epiphysitis, osteochondritis, and subchondral necrosis. It is now generally accepted that they all represent the same underlying pathological process, although there is no general agreement as to the exact etiological agent.

That some form of trauma with secondary vascular occlusion of the involved area is responsible is held by many. Embolic occlusion has also been mentioned as a cause, and endocrine dysfunction has been invoked by others.

TABLE I.—ASEPTIC NECROSIS (PARTIAL LIST)

Primary Centers

Vertebral body (Calve, 1925)
Carpal scaphoid (Preiser)
Semilunar, adult (Kienbock, 1910)
Patella (Kohler, 1908)
Astragalus (Mouchet, 1928)
Tarsal scaphoid (Kohler, 1908)
Medial cuneiform (Buschke, 1934)

Secondary Centers

Vertebral epiphysis (Scheuermann, 1921)
Sternal end of clavicle (Friedrich, 1924)
Head of humerus (Hass, 1921)
Capitellum of humerus (Panner, 1927)
Head of radius (Brailsford, 1935)
Ulna, distal (Burns, 1931)
Head of metacarpals (Mauclaire, 1927)
Iliac crest (Buchman, 1925)
Pubic symphysis (Van Neck, 1924)
Ischiopubic junction(Oldberg, 1924)
Head of femur (Legg, 1910)
Trochanter of femur (Monde Felix, 1922)
Patella (Sinding-Larsen, 1921)
Head of tibia (Ritter, 1929)
Tubercle of tibia (Osgood, Schlatter, 1903)
Os calcis (Sever, 1912)
Metatarsals (Freiberg, 1914)

The pathological process probably involves actual death of the ossifying nucleus, followed by fragmentation, irregular absorption of the involved bone, and replacement by so-called creeping substitution or recalcification. This is the same process that has been observed in adults, in whom aseptic necrosis is being increasingly recognized. In most instances the cartilage is not involved in the process. In general, the clinical findings are not prominent or acute, and there may be no complaints except slight pain and limping. There may be restriction of motion of the involved part.

The roentgen examination has been of the greatest aid in the study of the changing pathological picture in these cases, as by this method it is possible to demonstrate the early evidences of decalcification, the subsequent necrosis, and finally the signs of repair. In the earliest stages there are usually small areas of lessened density which increase in extent and intensity under observation. The epiphysis becomes fissured, fragmented, and fuzzy in outline, with a ragged appearance. Areas of dense necrotic bone are visualized. The process may involve both the epiphysis and the metaphysis, and the former may be compressed and flattened. In the stage of regeneration or recovery there is a gradual loss of the osteoporosis with absorption of the dense necrotic bone in the epiphysis. This is followed by slowly advancing replacement of the necrotic bone by recalcification, until there is complete bony restitution.

The amount of deformity of the restored bony contour will depend on many factors, including the stage at which it was first recognized and adequate treatment applied. The duration of treatment also plays a role. Some patients refuse to allow the involved part adequate rest after the symptoms have disappeared. It should be recognized that there is a definite lag in bony replacement as compared with the disappearance of the symptoms. Many patients have a definite sense of well being at a time when the roentgenograms still show necrosis and very little evidence of regeneration.

ROBERT P. MONTGOMERY, M.D.

Lewis, L. G.: Cases of Severe Pelvic Injury. *Ann. Surg.*, 1945, 121: 470.

Four cases of extensive pelvic injury from the armed services are presented. It is believed that when doubt exists as to whether ruptures of the bladder, urethra, and ureter exist, it is best to drain or divert the urine immediately. This procedure will save lives and lessen the morbidity.

Hemostasis in severe war wounds may be a serious problem. The repair of defects is desirable at the time of initial surgery to allow healing with minimum scar formation. If early repair is impractical, then sufficient time should be allowed for the subsidence of infection, healing, scar contracture, and for rehabilitation of the patient before corrective surgery is carried out.

In several patients who suffered from severe pelvic injuries complicated by rupture of the bladder and membranous urethra, excellent results were brought about when repair of the defects was carried out at the time of the initial surgery.

RICHARD J. BENNETT, JR., M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Wenger, H. L.: Transplantation of the Epiphyseal Cartilage. *Arch. Surg.*, 1945, 50: 148.

The proximal epiphyseal cartilage from a fibula containing a portion of diaphysis was successfully transplanted to the first metatarsal bone shortened by osteomyelitis. The toe, which was greatly shortened prior to the operation, was immediately corrected by the transplant. Observations made over approximately three years show that the transplant has "taken" and is functioning physiologically. The metatarsal bone in the foot which was operated on is of exactly the same size as the corresponding bone in the opposite foot. The proximal portion of the epiphysis appears to have fused with the cuneiform bone without impairing the growth of bone, which takes place more distally.

The eventual fate of the transplant cannot be prophesied at this time, but the extremely gratifying results obtained to date give assurance that this procedure is valuable.

ROBERT P. MONTGOMERY, M.D.

Straub, L. R., Thomson, T. C., and Wilson, P. D.: The Results of Epiphyseodesis and Femoral Shortening in Relation to Equalization of Limb Lengths. *J. Bone Surg.*, 1945, 27: 254.

The authors have evaluated the results in 89 cases in which epiphyseodesis was performed and in 19 cases in which femoral shortening was done for equalization of limb lengths.

An analysis of the 89 cases of epiphyseodesis showed that in 50 per cent a final limb discrepancy of 2 cm. or less was present and therefore the results could be considered satisfactory from a clinical standpoint. Growth deformity from unequal arrest of the epiphyseal growth following operation was found in 20.7 per cent of the cases.

In the 19 cases of femoral shortening, the average correction obtained was 4.7 cm. (1⅞ inches). There were no instances of delayed union, malunion, or nonunion. Complications occurred in 3 cases; in 2 there was infection and in 1, an ossifying hematoma.

On the basis of their results the authors conclude that the problem of limb equalization must be individualized and that no particular rule or procedure will provide the solution for all cases. They have found that epiphyseodesis, although apparently a simple procedure, is irreversible and presents the danger of growth deformity. The operation is of value in young patients who have a rapidly increasing discrepancy and a considerable difference in limb length. However, after the ages of eleven in girls and twelve and one-half in boys, little can be accomplished by this procedure.

Femoral shortening is a good procedure but limited in that the maximum correction obtainable is not over 3 inches. DANIEL H. LEVINTHAL, M.D.

FRACTURES AND DISLOCATIONS

Coyle, J. T., and Thompson, W. D.: Fractures in Battle Casualties. *Bull. U. S. Army M. Dept.*, 1945, 86: 57.

This is a report from a fracture service of a station hospital during a period of sixteen weeks ending November 1, 1943. It includes the entire Sicilian Campaign and about the first six weeks of the Italian Campaign. There were about 2,366 patients admitted to the surgical service, of whom 967 were battle casualties; 1,170 patients were evacuated, and 903 were returned to duty. The mortality rate was 0.3 per cent. There were 626 fractures; of these 493 were compound and the remainder simple. Foreign bodies were found in 161 cases of compound fractures by x-ray examination; 44 of these foreign bodies were removed at the time of operation. Among 626 cases of fracture, only 18 patients were found to have nerve injuries. Several secondary hemorrhages occurred from ten to fourteen days after injury. The position of the bones following fractures of the femur and humerus and fractures of the hands or feet was routinely poor on arrival; the position in fractures of the radius, ulna, tibia, and fibula was routinely good. Patients with fractures of the femur which had been put in body spica casts traveled more comfortably than those in the Tobruk splints. Patients with shoulder spica casts traveled comfortably with the fragments in better alignment. The split cast is more satisfactory than the bivalved cast. A few cases in padded molded plaster casts arrived in excellent condition. Suspension, traction, and indirect traction methods were used; both forms were successful.

Open reduction and internal fixation were performed on 24 selected simple factures with good results. Seventy-eight per cent of the split-thickness skin grafts were successful. Secondary closures were performed in 7 wounds over compound fractures and 80 per cent were successful.

RICHARD J. BENNETT, JR., M.D.

Branch, H. E.: Bullet Fractures of the Long Bones. *J. Bone Surg.*, 1945, 27: 227.

The purpose of this article is to emphasize the importance of conservatism in the debridement and management of bullet fractures of the long bones. The term "bullet fracture" is used to denote a compound shattering of a long bone, caused usually by a bullet or a fragment of metal casing from an explosive missile. The fracture resulting from a direct hit by a high-velocity bullet is typical, and is characterized by multiple small fragments of bone in a compound wound.

Three principles of wound treatment, such as (1) removal of only those bony fragments which are completely separated from the periosteum; (2) the placing of dressings loosely in the wound; and (3) complete and prolonged immobilization, are of particular importance. Loose and completely detached particles of bone should be removed, but bony fragments with periosteal and soft-tissue attachment should be left undisturbed. Nonmetallic foreign bodies which are readily accessible should be removed, but a search for all metallic particles is unnecessary.

After conservative débridement, a fine-mesh gauze pack, heavily impregnated with vasoline, should be loosely inserted at the bottom of the wound. The affected parts should be completely immobilized for a long period, and, occasionally, traction in plaster is necessary to maintain the length of the bone. Changes of cast should be infrequent.

Illustrations show the restorative powers of bone healing of which Nature is capable, if not interfered with unwisely. EMIL C. ROBITSHEK, M.D.

ORTHOPEDICS IN GENERAL

Kennedy, R. L. J.: Precocious Skeletal Development. *J. Am. M. Ass.*, 1945, 127: 580.

In 3 of 23 cases of precocious skeletal development a proved adrenocortical tumor was present. In 12 cases hyperplasia of the adrenal glands was either proved or, because of the clinical and laboratory evidence, was believed to be present. Three patients had been treated with endocrine preparations and it is possible, although not certain, that the precocious skeletal development was a result of the treatment. Finally, 5 patients did not have apparent cortical disease.

It is evident that precocious skeletal development is not a peculiarity of any single clinical syndrome. Although it was found in some cases of adrenocortical disease with increased excretion of 17-ketosteroids, in other cases of the same condition skeletal development was within normal limits. The cases studied indicate that precocious skeletal development may be found with or without obvious endocrine disorders, and that it may follow the administration of endocrine preparations.

Hendryson, I. E.: An Evaluation of the Estimated Percentage of Growth from the Distal Epiphyseal Line. *J. Bone Surg.*, 1945, 27: 208.

The difficulty of estimating the expected growth of a long bone is stressed more and more by the increased interest in the problem of equalization of length of the lower extremities, particularly in considering the operation of epiphyseodesis. Digby measured a set of long bones, and established a standard scale of growth from distal and proximal epiphyseal lines. Bisgard and Bisgard substantiated his findings by experimentation with animals. Wilson and Thompson then applied the same figures clinically in an effort to determine the expected growth in an extremity. By estimating the percentage of growth from each epiphyseal line, they made correction by epiphyseodesis (Phemister).

The author's study includes measurements made on 54 adult, human femora, selected at random from dried anatomical laboratory specimens. Of this number, 48 had a single nutrient canal, while 6 were discovered to possess two such canals. Two femora from the newborn were secured and identical studies made on them.

In making the measurements of the femora it was decided that more exact data could be secured by making roentgenograms of the bones and measuring them. This procedure was carried out by first passing a small needle along the nutrient canal and then mounting the bone on a cassette with clay so that roentgenograms could be made. In each case the rays would pass to the canal at a right angle.

Regular, ultraspeed film was used in making the roentgenograms. Exposures were made at 72 inches, with 75 peak kilovolts and 20 milliamperes, for fifteen seconds.

In determining the location of the metaphysis it was noted that after closure of the epiphysis a suitable variation in density did not always appear to reveal the site of closure. Two specimens in the group revealed epiphyseal lines which were nearly obliterated. From these, points were found which were present in all of the specimens, and which showed definitely the plane where the metaphysis and epiphysis fused.

It then became possible to measure the overall length of the shaft, and the distance between Digby's "site of initial ossification" and the distal and proximal ends of the shaft.

The author concludes that the Digby method of determining percentage of growth from a given epiphyseal line in a long bone (by comparing the diaphyseal length with the distance from the metaphysis to the intersection of the nutrient artery and the center of the medullary cavity) is unreliable and without foundation. The figures derived by the use of this method in estimating the percentage of growth from a given epiphyseal line are inaccurate.

ROBERT P. MONTGOMERY, M.D.

Batterman, R. C.: The Treatment of Arthritic Pain with Demerol, a New Synthetic Analgesic. *Ann. Int. M.*, 1945, 22: 382.

Demerol approaches the potency of morphine, but the addiction liability is much less than in any opiate derivative. Furthermore, demerol has been administered for many weeks or months without increase in the dosage to achieve the same analgesic effect. During the past four years, 183 hospitalized patients and 73 ambulatory patients were treated with demerol. All of these patients were suffering from severe pain associated with an arthritic condition. Eighty-nine patients received 92 trials of demerol parenterally, and 122 patients received 132 trials orally. Both methods were used in the treatment of 28 patients.

Parenterally administered demerol resulted in satisfactory analgesia in 83 per cent of the trials, and a further 13 per cent of the patients received moderate relief of pain. The administration of 100 mgm. parenterally every four hours was sufficient to control the pain for three or more hours in the majority of the patients. Few or no untoward reactions were noted. This same result was achieved as long as the medication was given at regular intervals. Excellent results were obtained in relieving the pain of the sciatic syndrome regardless of causation. Satisfactory results were also observed in patients suffering from myositis, acute bursitis, advanced osteoarthritis, and rheumatoid, gonococcal, and nonspecific infectious arthritis. Completely satisfactory results were obtained in 62 per cent of the 132 trials when demerol was given orally. The condition of the ambulatory patients was complicated by the fact that a high percentage experienced dizziness, nausea, vomiting, and, rarely, syncope. Of 73 ambulatory patients 29 did not obtain relief from pain. Some of these unsatisfactory results may have been due to the fact that the medication was not continued accurately or the dosage was not sufficient. Tolerance to the side reactions usually develops quite rapidly. This allows the analgesic effects to take place.

It is recommended when starting the use of demerol for ambulatory patients to start with a small dose, usually 25 mgm. for the first few days, until the tendency to reactions subsides. As soon as possible the dosage should be increased to 50 or 100 mgm. every four hours. This regime invariably gives satisfactory results regardless of the type of arthritis or the severity of the pain. Demerol can give symptomatic relief of pain only.

RICHARD J. BENNETT, JR., M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Scheinker, I. M.: Vasothrombosis of the Central Nervous System; A Characteristic Vascular Syndrome Caused by a Prolonged State of Vasoparalysis. *Arch. Neur. Psychiat.*, Chic., 1945, 53: 171.

Vasoparalysis and vasothrombosis of the central nervous system are discussed in this article, and 2 cases with evidence of progressive disorder of the nervous system on a vascular basis are reported. Autopsies on these 2 patients revealed both vascular lesions and changes in nerve tissue proper.

The vascular lesions consisted of maximal dilatation and congestion of the capillaries and small veins. They were engorged, and showed all the characteristics of vasoparalysis. There was also some degenerative change in the walls of the smaller blood vessels, advancing even to the point of complete necrosis with increased permeability for serous fluid and red blood cells. There was also manifestation of early thrombosis, and the lumens of some of the small veins were completely occluded with blood clots composed of curved strands of fibrin mixed with large masses of platelets and white blood cells. In these cases the vessel walls seemed to be well preserved, except for slight loss of stainability of the cellular elements.

The changes noted in nerve tissue were considered secondary to the circulatory change, and consisted chiefly of widely disseminated areas of softening, involving the cortical ribbon and the white substance. There were occasional small disseminated foci in the white matter.

The author considers that these changes, i.e., vasoparalysis and vasothrombosis (which is a later stage of the process), result from a slowing up of the cerebral circulation, in contrast to the etiological factors in thrombosis of arteries. It is not believed that any change in the vessel wall is necessary as an initiating factor of thrombus of the small veins.

Mechanical factors in the blood stream favoring a slowing up of circulation result in an accumulation of red blood cells and platelets with the gradual production of a thrombosis. The state of vasoparalysis, associated with extreme dilatation of the smaller veins, is the precursor of such stasis and is followed by vascular occlusion. HOWARD A. BROWN, M.D.

BLOOD; TRANSFUSION

Barker, N. W., Cromer, H. E., Hurn, M., and Waugh, J. M.: The Use of Dicumarol in the Prevention of Postoperative Thrombosis and Embolism, with Special Reference to Dosage, and Safe Administration. *Surgery*, 1945, 17: 207.

This report is based on observations of 1,000 surgical patients who were given dicumarol [3,3′—methylenebis—(4 hydroxycoumarin)] in their immediate postoperative period for the purpose of preventing venous thrombosis and pulmonary embolism. The authors have found this drug effective in the prevention of these complications in patients who have had nonfatal pulmonary embolism, thrombophlebitis, or a history of previous thrombosis or embolism; and when this drug was given prophylactically, no thrombosis or embolism occurred. Dicumarol should not be used unless daily and consistently comparable prothrombin-time tests are made, since without these it is impossible to be certain whether insufficient, adequate, or excessive, and possibly dangerous, amounts have been given. The authors believe that only the Quick prothrombin-time test should be used for these determinations. Consistently comparable prothrombin-time tests depend on the use of thromboplastins of constant potency or on the checking of each new batch of thromboplastin with various dilutions of normal plasma. It may be preferable from the standpoint of the clinician or surgeon who is supervising the administration of dicumarol that the reports be given in percentages of normal prothrombin rather than in seconds.

The experience of the authors in the 1,000 cases in which dicumarol was used has been that, with the thromboplastic substance which was used, thrombosis or embolism almost certainly did not develop if the prothrombin time was greater than twenty-seven seconds, the time which corresponded to that of 30 per cent normal plasma, and that definite bleeding did not occur if the prothrombin time was less than sixty seconds, the time which corresponded to that of 10 per cent normal plasma. The authors have adopted arbitrarily thirty-five seconds, the time for 20 per cent normal plasma, as the key point in deciding about the dosage.

Dicumarol is effective when administered orally. The authors have endeavored to simplify the plan of administration as far as possible in order to keep the prothrombin level between 30 per cent and 10 per cent of normal for each individual patient, and they recommend the following plan of dosage:

The entire amount of the drug for each day is given in a single dose. Three hundred milligrams are given the first day and 200 mgm., the second day. Two hundred milligrams are given on each succeeding day that the prothrombin is greater than 20 per cent of normal. If it is less than 20 per cent of normal, no dicumarol is given on that day.

It must be re-emphasized that definite prothrombin deficiency does not develop immediately after the drug has been given. Effective levels are not reached until after from twenty-four to forty-eight hours, and sometimes a considerably longer time.

If, because of hemorrhage or abnormally high prothrombin times, it is deemed advisable to lower

the prothrombin time, this usually can be accomplished by the transfusion of 500 c.c. of fresh citrated blood. It may be necessary to transfuse blood several times over a period of two or three days, since there is a tendency for the prothrombin time to increase again after from two to six hours have elapsed.

In the course of this study menadione bisulfite, usually in a single dose of 64 mgm., was administered intravenously to 37 patients among whom an excessive deficiency of prothrombin had developed after the administration of dicumarol. All but 2 patients responded satisfactorily. The actual risk of bleeding is small among postoperative patients receiving dicumarol if the method of dosage and control mentioned previously is followed. It is particularly small among patients who have had some thrombotic or embolic episode.

Boynton, M. H., and Taylor, E. S.: Complications Arising in Donors in a Mass Blood-Procurement Project. *Ann. J. M. Sc.*, 1945, 209: 421.

A study of 40,000 donors has disclosed that, with a controlled basis of operations for all procedures and a rigid eligibility standard for all volunteers, the withdrawal of 500 c.c. of blood from normally healthy individuals offers no serious potential hazard.

Approximately 10 per cent of the donors have experienced transient discomfort in the arm from which the blood was withdrawn, and about 9 per cent have had some form of transient reaction during or immediately after the donation. The instances of delayed reactions or syncope some hours after the donation were rare.

The cardiovascular complications reported were fewer than the normal expectancy for accidents of this nature, and were evidently not directly related to the withdrawal of blood. Approximately 4 per cent of the donors experienced prolonged or late manifestations, the basis for which may have been a delayed regeneration of the hemoglobin. Only a very small group developed symptoms for which there was no apparent physical basis.

WALTER H. NADLER, M.D.

DeGowin, E. L.: Isoimmunity to the Rh Factor as a Cause of Blood Transfusion Reactions. *J. Lab. Clin. M.*, 1945, 30: 99.

The author presents a short history of the work done in studies of the agglutinin factor, designated by the initials Rh, and notes that some individuals whose blood is Rh-negative would seem to possess the potentiality of developing anti-Rh agglutinins by either of two mechanisms: by receiving blood in repeated transfusions from Rh-positive donors or by bearing children whose blood is Rh positive. Since approximately 15 per cent of persons of the white race in the United States have blood which is Rh-negative, it might be considered that the development of isoimmunity to the Rh factor would be a common phenomenon through either of the two mechanisms. Actually, although the combination of the Rh-positive child and the Rh-negative mother occurs in about 1 of 10 pregnancies, only 1 pregnancy in 400 results in hemolytic disease of the child. It has also been noted that not all Rh-negative recipients are immunized by repeated transfusions of Rh-positive blood.

It is particularly desirable to obtain some perspective on the incidence of isoimmunity in a general transfusion service because the prevention of transfusion reactions due to the anti-Rh agglutinin requires special laboratory tests preliminary to transfusion. The military employment of multiple transfusions of group O donors to recipients of any blood group without preliminary cross-matching also raises the question of possible mortality from isoimmunization to the Rh factor.

The author discusses the methods of the investigation that have led to the report herewith presented. The incidence of reactions is noted and classified. A series of 5,386 consecutive blood transfusions was studied. Of these, 5,200 transfusions were given without reactions. There were 186 (3.4 per cent) transfusions with reactions of all types. Of these reactions, 101 (1.8 per cent) were of the chills and fever type. Of the total reactions of all types, only 6 could be attributed to isoimmunity to the Rh agglutinogen, an incidence of 0.1 per cent. Sensitization to the Rh factor was attributed to multiple transfusions in 4 instances; pregnancies were responsible in the other 2. There was 1 fatality.

The author presents in detail the case histories of the patients showing isoimmunity to the Rh factor, and discusses the clinical manifestations of transfusion reactions due to isoimmunity. The difficulties in testing for Rh incompatibilities are presented and discussed.

In conclusion, it is noted that a series of 5,386 consecutive blood transfusions was studied. Multiple transfusions were given to recipients without regard to Rh type or to obstetric history of female recipients. Transfusion reactions of all types were studied for evidence of isoimmunization with the Rh factor. The incidence of transfusion reactions of all types in the series was 3.4 (0.2 per cent). In 3,132 transfusions given to 1,112 males, the incidence of reactions was 3.1 (0.2 per cent). In 1,004 female recipients of all ages, the incidence of reactions was 3.9 (0.4 per cent) in 2,254 transfusions. This is considered to be a statistically significant difference in the sexes which may possibly be explained by isoimmunity to the Rh factor developed during pregnancy.

In the 186 transfusion reactions of all types, only 6 were found which could be attributed to isoimmunity to the Rh factor, an incidence of 0.1 per cent in the 5,386 transfusions. Isoimmunity was attributed to multiple transfusions in 4 instances and to pregnancy in 2. There was 1 fatality from transfusion of Rh-positive blood to a recipient who had been sensitized by multiple transfusions.

There were 1,717 recipients receiving from 1 to 3 transfusions. In this group, none was sufficiently

sensitized to the Rh factor to give clinically significant reactions. It is estimated that of the 399 recipients receiving 4 or more transfusions, approximately 60 were Rh negative. Only 4, or 6.6 per cent, of these were immunized to the Rh factor by multiple blood transfusions.

The case histories of the 6 recipients with isoimmune reactions are reported. Preliminary crossmatching for the anti-Rh agglutinin would not have prevented all of the reactions. A series of increasingly severe reactions in a recipient cannot be depended upon as adequate warning of developing sensitivity to the Rh factor.

HERBERT F. THURSTON, M.D.

Self, E. B., Thalhimer, W., and Scudder, J.: Pooled Human Serum. *Ann. Surg.*, 1945, 121: 338.

The authors present a report on the administration of 297 units of human serum to 136 different patients. They note that the consensus of opinion appears to be that serum is equally as effective as plasma, although associated with a higher incidence of reactions. The quantity of serum administered at a single injection by the authors varied from 50 c.c. in a few babies to a maximum of 4,000 c.c. in a burn case. The total amount given in several infusions to 1 patient was 5,850 c.c. The average dose of serum per case was 580 c.c.

The authors describe in detail the 136 cases in which serum was used for shock due to skeletal trauma, shock due to hemorrhage, operative and postoperative shock, for the treatment of burns, septic conditions, hypoproteinemia, and for prophylaxis. The incidence of reaction was 27.5 per cent for 244 transfusions of serum. There was little difference between the reaction rate for the liquid and the dried product.

The following deductions are made by the authors from this study: (1) fresh liquid serum gave consistently a 100 per cent chill-fever reaction rate (what this toxic factor is in fresh serum which disappears on aging is not known); (2) liquid serum prepared by concentration in cellophane bags gave such severe reactions in 3 of the 6 patients that the remaining 7 bottles of serum were not used; (3) the chill-fever reaction constituted the largest group—13.9 per cent; (4) the 10 severe reactions which required stopping of the serum transfusion or immediate supportive therapy included 2 which occurred during administration of the concentrated liquid serum.

In this series no fatality was attributed to the giving of serum. Reactions practically never occurred in patients being treated for shock. The total reaction rate, excluding the fresh serum, the concentrated liquid, and the reworked serum, was 24.6 per cent.

The authors emphasize that they believe both plasma and serum have a place in the treatment of patients. From their experience, plasma and serum are equally efficacious clinically. They can be used interchangeably without noticeable difference. Each possesses certain advantages which the other does not possess, as follows:

In plasma, (1) there is a lower incidence of reactions; (2) there is a greater yield; (3) plasma contains fibrinogen and prothrombin; and (4) it is more easily prepared as a by-product of a blood bank.

In serum, (1) there is greater protein content, and pools contain 7 gm. per cent as compared to 5 gm. per cent for plasma; (2) the expense and trouble of citrate is obviated; (3) serum can be filtered; hence, bacterial sterility can be assured; (4) liquid serum remains clear, while plasma (unless recalcified) precipitates fibrin; and (5) drying is easier without the presence of citrate.

In conclusion, the authors note that pooled human serum is an effective blood substitute. Serum administration is associated with a definite incidence of reaction, greater than that with plasma. In their experience, fresh serum, prepared and injected within twenty-four hours of the drawing of the blood, gave a severe chill-and-fever response in each case. Serum is now being prepared at the Presbyterian Hospital Blood Bank to meet the need of supportive therapy in patients with low plasma proteins and low calcium. Massive replacement with serum rather than with citrated plasma theoretically is safer in such states, particularly in infants. The reactions caused by either serum or plasma are rarely severe; the choice between them becomes largely a question of convenience as well as practicability of preparation and administration.

HERBERT F. THURSTON, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Leavell, B. S.: Acute Heart Failure following "Blast Injury." *War Med.*, Chic., 1945, 7: 162.

In 3 cases apparent congestive heart failure following blast injury was observed in patients with previously normal hearts. Thirty-five other patients with blast injury were studied from a cardiovascular viewpoint. Two of these had abnormal venous pressures without obvious cause, and 3 additional patients manifested definite electrocardiographic abnormalities.

Whereas at the present time no adequate explanation can be offered for these observations, the problem is worthy of further study, since it suggests that when pulmonary edema develops following blast injury, digitalization and venesection may be indicated. JOHN J. MALONEY, M.D.

Dick, I. L.: The Management of Multiple Injuries in Aircrews. *Edinburgh M. J.*, 1945, 52: 61.

In an article dealing with aircrew casualties the author discusses 3 types of injuries: (1) gunshot and missile wounds; (2) burns; and (3) fractures and fracture-dislocations.

The first group is relatively insignificant since it is indistinguishable from similar injuries inflicted under other circumstances. What is more, two factors serve appreciably to lessen grave complications, namely, efficient early treatment and absence of gross contamination of the wounds.

Burns constitute a very specialized problem. Practically always the unprotected hands and face are involved. When these burned areas do not heal rapidly with minimal contracture, serious disability ensues. Increased fibrosis and consequently greater contracture are a direct result of prolonged granulation. The problem, therefore, in the treatment of burns of the hands and face is to control infection and to replace lost skin without delay. Moreover, function of the hands must be preserved. It often happens that joints are opened and tendons destroyed, which involves prolonged granulation. Measures must then be taken to prevent impairment of the function of the hand by preventable contracture.

At the beginning of this war the application of tannic acid or some other form of coagulant was almost universally used in the treatment of burns. While this is still adequate treatment for many types of burns, it proves disastrous in the treatment of burns of the hands and face. The coagulant treatment of burns depends for its success on the maintenance of sterile conditions under the coagulum. Then only can it be used without causing harm. In burns of the face, even without tissue destruction, some degree of infection must occur, and treatment must be directed to its control. In third-degree burns of the face and elsewhere, controlled infection is a valuable part of the healing process, since without it, sloughs separate much more slowly. Although infection serves a useful purpose while the sloughs are separating, it must be eliminated at the stage of re-epithelization of the burn. Epithelium will grow with amazing speed if the obstacles to its growth are removed. These obstacles are infection and irregular granulations.

For burns of the face the author recommends daily saline irrigation, if possible in a saline bath, and dressings of sulfonamide powder, tulle gras, and saline packs until every slough has separated. As soon as infection is under control, the remaining raw areas are covered with a split-skin graft. This minimizes contracture and the need for subsequent plastic repair. Particular care must be given to the eyes, since contracture around the eyes causes exposure of the cornea. This, in the presence of infection, results in corneal ulceration with loss of the eye. In all cases in which the eyes are involved, penicillin is now instilled into the conjunctival sac; this saves the eyes which would otherwise be inevitably lost.

The rules governing the treatment of burns of the hands are in exact accord with surgical first principles. They are: control infection, promote healing, prevent contracture, and, above all, preserve function. Hands should be treated with daily saline baths and with sulfonamide, tulle gras, and saline packs bandaged on so that the fingers can be moved and exercised from the beginning to preserve their function. So treated, they need not become stiff. The granulations are covered with a split-skin graft as soon as indicated. A temporary deterioration in finger movement always accompanies the skin-grafting of a burned hand. This is due to the immobilization which must be established in order that the graft may take. It is soon overcome, however, since the period of immobilization does not exceed four or five days.

When the burn destroys tendons and open joints, another consideration must guide the surgeon in his treatment. Severe limitation of movement results from a burn of this degree, and what movement remains must be facilitated by the functional position of the hand and not hindered by preventable contracture. The author states that in the Royal Air Force the hands are usually burned worst on the dorsum, and the characteristic contracture of a severe burn of the dorsum of the hand fixes the metacarpophalangeal joints in hyperextension. Once this contracture has become established there is no known means of restoring any function whatsoever to the affected digits. The rarer burns of the palm produce a flexion contracture which is equally disabling. Hands thus gravely burned must be splinted, preferably in plaster, in the best functional position, with the metacarpophalangeal joints in midflexion, until a fibrous ankylosis occurs. The patient is encouraged to develop such movement of the hand as is possible.

It may not be much but it is useful movement with regard to function—and not the "pathetic flicker of a subluxated joint."

The third type of injury, fractures and fracture-dislocations, differs widely from the stereotyped burns of aircrews in its enormous multiplicity and extraordinary variety. In view of the force producing these injuries, the terrible stresses machines and men are subjected to in aircraft crashes, and the speed of impact in these crashes (which is seldom less than 100 miles per hour), it is not surprising that more than one injury in the same patient is frequently found. Severe displacements and compound fractures are common. Often head injuries dominate the immediate picture and delay the treatment of other injuries. Stupendous and multiple as these injuries are, two factors help greatly in the treatment of aircrew casualties, namely, the fact that these injuries occur usually in young fit men whose morale is high; and the fact that these injured usually come under treatment within a few hours. Thus combinations of injuries can be treated successfully which might under other circumstances prove fatal.

The treatment of multiple injuries is divided into two phases, the immediate and the definitive or more remote. The immediate phase takes care of general considerations consisting mainly in the control of shock, and local considerations consisting in the prevention of wound infection and the primary reduction and splinting of fractures. Fractures occupy a very secondary place in the immediate phase and must not be given undue emphasis. The definitive or remote treatment concerns itself with the management of wound healing, the replacement of skin loss, and the accurate realignment of fractures. In this phase all possible methods of fracture treatment should be available. Frequently a program of suitable treatment of an individual injury must be discarded because of unavoidable delay in starting it, infection, or other injuries in the same limb or elsewhere.

Immediate attention must be given to shock, which is one of the most treacherous and deceitful conditions. It is important to emphasize the caution that severely shocked patients should be lifted and moved as little as possible. They should always be taken from the ward to the theater in bed and not on a trolley. One lift from the bed to the table is enough, and they should be lifted with scrupulous care and gentleness. It is likewise important that severely shocked patients should not necessarily be moved to a hospital as soon as they are seen at the site of the accident. It is easier for a patient to stand a short journey to a nearby place of shelter where he can be given plasma and blood and left to recover until he is fit to move further, for he may die in the ambulance if he is taken straight away on an hour's journey.

Treatment of shock may be epitomized very briefly in the use of measures to restore the normal volume of the circulating blood. The first step is to get a blood-pressure reading and to begin plasma transfusion. The blood-pressure reading is made to serve as a base line against which further readings can be compared. Blood-pressure readings are the most valuable indication of the degree of shock and the effect of resuscitation. Reliance cannot be placed on one blood-pressure reading alone. An accurate estimate of the patient's condition demands a close follow-up to determine whether the blood-pressure is stationary, rising, or falling. There is a stage of vasoconstriction in shock when the blood pressure is high and sudden and dramatic alterations may occur without warning. Transfusion, therefore, is started immediately, for, once the needle is in the vein, shock is largely under the control of the surgeon. Plasma can be used without any typing or crossmatching, and is as efficacious as blood in restoring the blood volume in the initial stages of resuscitation. In the stage of hemoconcentration, transfusion of up to 2 pints of plasma not only restores the blood volume but brings again into active use red cells which were stagnant in dilated capillaries.

For massive transfusions it is not desirable to use plasma since (1) a transfusion of more than 2 pints of plasma causes hemodilution, and then plasma becomes much less effective in controlling shock than whole blood; (2) the administration of large amounts of plasma is followed in two or three weeks by a very troublesome and intractable secondary anemia; (3) large amounts of blood are lost into the tissues in closed fractures without any external bleeding. Thus, for example, from 1½ to 2 pints of blood may be extravasated into the muscles of the thigh in the presence of closed fracture of the femur.

For massive transfusions, blood is used. Three- or 4-pint transfusions are relatively common. An empirical limit must not be set to the amount of blood which should be given to any patient. Grave injuries in which there has been a heavy loss of blood sometimes demand up to 10 and 12 pints. After the blood transfusion is begun the blood pressure should be recorded and charted at fifteen-minute intervals so that sudden deterioration of the patient's condition may not escape recognition. This can be done while preparations for operation are in progress and can be continued every ten or even five minutes during the operation. The medical officer in charge of the case must keep most careful watch so that any sudden drop in the patient's condition may be promptly met by speeding up the transfusion.

Great importance attaches to the anesthetic and to the method of its administration. The anesthesiologist is a key member of the surgical team, and precise judgment and great care must be exercised by him in the procedure. Spinal analgesia should never be used in these cases since it produces a drop in blood-pressure, and since its effect once established is not readily reversible, its use is too dangerous. Local anesthetics are usually excluded by the technical difficulty of the multiple infiltrations needed and by the potential or actual infection of the wounds. Sometimes, however, regional blocks may be used with advantage. Gas and oxygen given by an

expert, with especial care to avoid any increase in tissue anoxia, is the best means of maintaining anesthesia. A little ether or cyclopropane is added if necessary.

The most important object of the immediate local treatment of patients with multiple injuries is the control of infection. This is effected by careful and thorough excision of wounds, and the prevention of skin necrosis due to gross bony displacement.

As to fractures and fracture-dislocations, the immediate treatment of these injuries calls for a clinical reduction of the displacement so that the skin is preserved and the complication of sepsis is not added to the existing lesion. A limb in which there is a fresh or a recently manipulated fracture, or a recent wound, due either to accident or to operation, must not be enclosed in a complete plaster. The plaster should be split its entire length, and the dressings under it split down to the skin so that reactionary swelling cannot endanger the blood supply to the limb.

The definitive treatment of injuries can begin when the patient has recovered from shock, and his general condition warrants it. When there is no skin loss, wounds of almost any size will heal with remarkable rapidity under a closed plaster if infection is adequately controlled. Granulations soon fill up any defects in a properly excised wound and final healing soon follows. If infection persists in such a wound, it is due either to inadequate drainage of the wound and consequent pocketing, to sequestration of infected bone, or to a retained foreign body. The wound then needs further exploration with provision for free drainage and the removal of any foreign body or separated sequestrum.

When skin has been lost the procedure is different. Any tissue loss under the skin is made good by granulations which fill the defects and contract into a firm scar, but until the granulation tissue is covered with skin the wound is not healed. To promote rapid healing of a wound the answer lies, as in the burn, in the control of infection and the replacement of lost skin by a skin graft. Usually quite simple forms of skin-grafting are sufficient. Epithelium will grow over only flat uninfected granulations. The wound should be covered in plaster until the granulations are flush with the surface. Then the raw area is prepared for the reception of skin by exactly the same method as that used in the treatment of burns.

The treatment of bone and joint injuries follows the ordinary methods. In aircrew injuries the severity and multiplicity of deformities are often tremendous. Massive bone grafts are often needed to replace lost bone or to provide internal fixation for a fracture of which the alignment could not be controlled by external splints and which could not be treated by early operation because of a wound. A bone graft is essential for the first of the two purposes, and it is much better than a metal plate for the second, as it promotes union in addition to providing internal fixation of the fracture.

A common type of injury in aircrews is fracture of the spine. Specific search must always be made for injury to the vertebral column alone or as an associated lesion in patients involved in aircraft crashes even when no complaint is made of pain in the back. Also, the spines of patients with fractures of the os calcis or astragalus, no matter how they were injured, should always be examined as a fixed routine. Severe pain in the foot often masks minimal discomfort in the back. There may be an obvious, gross and dramatic injury elsewhere, but the spine of a patient injured by severe violence must always be examined before a course of treatment is planned.

MATHIAS J. SEIFERT, M.D.

Ross, J. A.: Removal of Projectile Fragments and Immobilization of Wounds. *Brit. M. J.*, 1945, 1: 330.

Immobilization is an extremely important part of transportation of the wounded. Gunshot wounds of the vertebra should be immobilized in a padded posterior shell. In fractures of the acetabulum and upper third of the femur a Whitman plaster cast should be applied. Compound fractures of the tibia should be immobilized in a plaster cast which runs well above the knee. Penetrating or perforating wounds of the foot should be immobilized in plaster casts. One hundred per cent of all compound fractures of the os calcis arriving in South Africa required amputation. Wounds of the wrist and forearm require padded, split plaster casts with immobilization of the joint above and below the site of fracture. Wounds of joints require immobilization Elevation of an extremity enclosed in a plaster cast cuts down materially upon edema and constriction. On the other hand, excessive splinting has done much harm by causing stiffness of the joints of the hand. One word of caution must be given: when extremities are put up in plaster casts or splints, gas gangrene must always be thought of as a possible complication.

RICHARD J. BENNETT, JR., M.D.

Byrne, R. V.: The Healing of Wounds in New Guinea. *War Med.*, Chic., 1945, 7: 181.

Fifty cases of surgical wounds were studied under tropical conditions from the standpoint of the normal healing of wounds in the tropics. Of the 50 wounds, 4 were infected. In 3 of these 4, the infection was due to a break in surgical technique. In 1 case there was an obvious infection in a clean wound. The operations were performed at an advanced naval base hospital under typically tropical conditions. The operating room was exposed to dirt and dust, but it was comparatively bug proof. Cotton sutures were used in all except 1 case, as experience has shown that the reaction in the tissues conforms more to the normal healing processes when cotton rather than surgical gut is used. Careful handling of the tissues was considered of the greatest importance, and every effort was made to protect them. In the cases studied there was no evidence which suggested that clean wounds do not heal well in tropical climates. JOHN J. MALONEY, M.D.

White, J. C., and Scoville, W. B.: Trench Foot and Immersion Foot. *N. England J. M.*, 1945, 232: 415.

Even since the epic retreat of the Greeks under Xenophon across the snow-capped Armenia mountains, frostbite and kindred injuries to the feet from cold have been reported in the literature. Cold does not necessarily produce a single type of injury but instead results in several distinct syndromes which become most important when clothing, food, heat, and shelter are likely to be inadequate and when a great number of indoor dwellers are exposed to the rigors of outdoor life. Wet cold is far more difficult to deal with than the more severe degrees of dry frost, a finding made by the American medical officers with the troops who landed on Attu.

The two conditions to be considered here—trench foot, and its seagoing counterpart, immersion foot—are both caused by prolonged exposure of the dependent lower extremities to cold and moisture. The knowledge of trench foot is acquired from army surgeons who attended many of the Aleutian casualties of this war and who have made their data and criticisms available. The immersion-foot information was obtained through personal experience with survivors of torpedoed vessels who were exposed to cold water during a prolonged period while adrift in the North Atlantic.

Survivors in a crowded lifeboat are forced to sit with their feet dependent and immobile. This alone produces edema and if starvation with its hypoproteinemia is an added factor, the edema often is pronounced without cold. Occasionally when a man is forced to kneel or sit for prolonged periods on the bottom of a rubber raft, this same condition is seen involving the knees and buttocks. In the Aleutian landings men were forced to take cover in foxholes in a semisitting position from three to fourteen days in melting snow by day and light frosts at night. During this period they had little to eat, were chilled thoroughly, and had no opportunity to change footgear. Under these conditions all the circumstances leading to tissue damage in a crowded lifeboat are present ashore—exposure of legs to cold just above freezing, wetness, dependency and immobility, and general chilling of the body.

Immersion foot and trench foot differ from frostbite simply because the tissues are not actually frozen. There are no ice crystals in the tissues above the freezing point of sea water, mud, or thawing

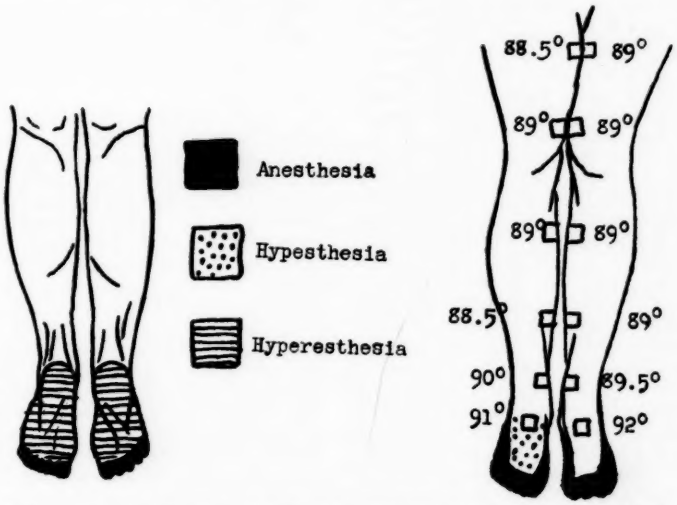


Fig. 1. Sensory changes and surface temperatures in a case of immersion foot. Moderate hyperemia and anesthesia, without much cutaneous injury, two weeks after rescue. Appearance of feet: redness of skin and petechial hemorrhages. Redness most striking in dependency. Very slight residual swelling. Superficial loss of epithelium on soles. Arteries: All pulsations strong. Veins: very prominent. Sweating: began slightly over skin of proximal feet at thirteen days. Neuritis: +++, beginning to subside. Sensation: touch, vibration, and detection of figures present except in toes. Two-point discrimination slightly reduced over dorsum of feet, absent in toes.

	T_1	T_3	T_5
R:	89°	88.5°	88.5°
L:	89°	88.5°	89°

Room: 70.5

snow, but from this temperature up to 50°F. the feet gradually become chilled, numb, and swollen. Experimental lesions similar to trench foot and immersion foot have been reproduced in rabbits and in the tails of rats. In sailors adrift at sea these changes may begin in the course of a few hours, but in the trenches where feet get wet and chilled more slowly several days of exposure may be necessary. The condition at sea differs from trench foot because the men in a crowded lifeboat do not have the opportunity to walk and thus to traumatize their numbed feet. If trauma occurs, infection usually follows and often ends in moist gangrene. In 231 cases of trench foot treated in the Aleutian campaign amputation of one or both feet was required and in 18 cases the greater part of one or more toes was lost. At another hospital 27 of 35 severe cases from Attu required late plastic operations. After sea exposure, infection and gangrene are fortunately less frequent—only 1 of 100 patients lost his leg and 2 patients suffered the loss of one or more toes. This has led the authors to conclude that trench foot causes more extensive and severe damage to the tissues than does immersion foot.

When first seen after exposure in either condition, the feet are cadaveric in color, swollen, and blistered. Massive gangrene from the ankle may appear imminent, but when there is no infection and proper treatment is administered the recovery capacity is amazing. Recovery takes place in two stages, an early hyperemic stage, and a later period of fibrosis. If the exposure was prolonged, incapacity may be present in both phases.

The hyperemic phase develops as soon as the legs become warm and circulation recovers. The absorption of damaged tissue causes a vasodilator response. There are bounding pulsations in the deep vessels and heat radiating to the surface makes the skin fever-hot (Fig. 1). In addition, the superficial circulation may be profoundly impaired, as shown by petechial hemorrhages from ruptured capillaries and thromboses of the subcutaneous blood vessels. Increased capillary permeability results in extravasation of protein-rich fluid that cannot be removed by the injured lymphatics. This accounts for the edema, blistering, and later fibrosis. The heat which raises metabolic demands of the cells for oxygen and the inadequate superficial circulation results in cutaneous anoxia and burning pain as soon as the nerves recover. This sensation recovery takes place rapidly in the proximal parts of the feet, but in severe cases, the toes may remain anesthetic for weeks.

In from one to four weeks the hyperemia subsides, and the circulation returns to normal, the blebs absorb, and the skin peels with a certain amount of scarring. The patients with milder cases then can return to work, but in the severer cases the skin becomes atrophic, movement of the toes is limited, and walking is painful and difficult. Biopsies of the skin and superficial muscle of the feet in men incapacitated several months after exposure showed atrophy and thinning of the epidermis, intense fibrosis, and deposition of collagen about the nerve endings and subcutaneous blood vessels. The muscles were infiltrated and their fibrils separated by a network of scar tissue, the extent depending on the initial exudation of fibrin and tissue anoxia. It is reasonable to assume that this explains the late pain, rigidity, and weakness of the feet, a condition which improves after six to eight months when the collagen ceases to contract. In some of the worst cases pain has been troublesome for over two years. Other factors contributing to the disability are the weakness and deformities secondary to the long-continued immobilization and the hyperesthesia that may accompany the return of sensation after nerve injury. The role of malnutrition and avitaminosis should also be considered in the pathogenesis.

In treating these cases one must keep the patient off his feet and protect him against rupture of the blebs and the formation of pressure sores in the weight-bearing areas of the anesthetic skin. If streptococcal infection begins, moist gangrene and loss of the leg are apt to follow. The general effects of cold should be combated by warming the body with blankets and hot-water bottles and giving hot tea, coffee, or soup internally. A nutritious high-protein, high-vitamin diet should be given as soon as tolerated. If the vitality is low, Plasma transfusions to combat shock and hypoproteinemia are valuable.

The injured feet must be kept cool while the body is warmed. This can be best accomplished by exposing the legs to a cool room temperature and blowing air over them with a fan or blower. The feet should never be rubbed or painted with a strong disinfectant and aseptic precautions should be taken with sulfonamides and a "booster dose" of tetanus toxoid. Elevating the legs helps drain edema fluid and shrinks the blisters. Unless the excessive surface heat is reduced, cyanosis increases, blisters swell, and the pain becomes acute. This is due to an anoxia of the tissues and may lead to increased extravasation of fluid and necrosis of the skin.

Upon arrival of the patient at a base hospital the same local treatment should be carried out until the hyperemia due to absorption of damaged tissue has subsided and circulation through the thrombosed subcutaneous vascular bed recovers. The surface cooling should be pushed until pain is relieved and ideally a cutaneous temperature of from 75 to 70°F. should be reached. This cooling reduces the metabolic need for oxygen to a point where sufficient quantities can be supplied through an injured capillary bed. In severe cases cooling with room air may not suffice and ice bags may be necessary; care should be taken not to chill the toes too much.

If gangrene has already developed before the patient enters the hospital, periodic débridement and painstaking care of the feet are necessary. Extremities can be saved usually by conservative amputation of the toes and distal portions of the feet. Early amputation of a leg is excusable only in fulminating lymphangitis, threatened septicemia, or gas gangrene.

In some of the long-standing disabilities the interstitial scarring may result in rigidity and contractures of the toes as well as atrophy and weakness of the ligaments and intrinsic muscles of the feet. The pain is of two varieties—a burning, hyperesthetic type, probably due to irritation of nerve endings by scar tissue, and a dull ache in the arches and ankle joints, probably due to a combination of muscle weakness, disuse, rigidity, and fallen arches. These difficulties may be relieved to some extent by physiotherapy and orthopedic exercises.

A vast man-power saving could be achieved if this period of pain and rigidity could be shortened. Although sympathectomy is quite illogical in the early hyperemic stage, release of the vasoconstrictor tone would relieve the late disabling symptoms by hastening the absorption of collagen and fibrous tissue and by increasing the superficial and collateral circulation through the injured extremities. Some authors have reported the association of vasospasm with this condition and report dramatic improvement with sympathectomy. A limited number of cases with atrophic rigid feet and delayed wound healing with vasospasm showed gratifying results after lumbar sympathectomy. The authors believe that unilateral sympathectomy should be tried in bilateral severe trench foot with atrophy, rigidity, and fibrosis. It should be attempted in cases with and without vasospasm, and should be controlled by means of biopsy at the time of operation and three months later.

One of the authors saw many initially mild cases of trench feet after a considerable length of time had elapsed and was impressed with the susceptibility of these cases to hysterical prolongation of symptoms and the need for orthopedic correction of the mechanical dysfunctions.

Many of these cases of trench and immersion foot can be prevented in campaigning under winter conditions by prophylactic measures of foot hygiene, by improvement in protective clothing, and by safety measures at sea. Early emergency treatment determines how much of the foot and toes can be saved and how long the disability will continue.

ROBERT R. BIGELOW, M.D.

Lesser, A.: Report on Immersion Foot Casualties from the Battle of Attu. *Ann. Surg.*, 1945, 121: 257.

From his observations in the treatment of 52 immersion foot casualties, the author draws the following conclusions:

The most important provocative factors involved in the causation of these cases are: (a) increased susceptibility to lowered environmental temperature (but above freezing) as a result of increased conductivity of the constantly wet skin; (b) vascular stasis of the extremities as a result of prolonged periods of inactivity while the individual is lying in fox holes and ravines; (c) the effects of hypoproteinemia and vitamin depletion from lack of food on the capillary permeability; and (d) the effects of loss of blood in the patients who were wounded.

Most of the tissue injury presumably occurs during this so-called "thawing out" period; that is, when the wet shoes or boots were removed, there was a sudden flooding or choking of the tissues with fluid. Such "choking" of the tissues of the extremities with fluid is probably related to extensive vasodilatation, possibly the result of the accumulation of a toxic histaminelike substance in the tissues, as well as other provocative factors of the immersion period. Thrombosis of smaller-sized blood vessels is undoubtedly related to the sudden increase in pressure within the tissues of the extremities. The extent of tissue necrosis and gangrene is obviously dependent upon the extent and severity of the choking of the tissues and the thrombosis, and the degree of recanalization of the end vessels of the extremities. The deposition of large amounts of fibrinogen-rich transudate, and of collagenous and fibrous material is eventually responsible for contractures, hardening, and pain in the soft tissues of the feet and toes.

The therapeutic implications are concerned with the prevention or control of the severe outpouring of fluids or transudate into the tissues of the extremities. The measures which suggest themselves are: (a) elevation of the lower extremities; (b) immediate application (on removal of shoes or boots) of a pressure-dressing support to the extremities in the form of Ace bandages, gum-rubber bandages, Unna's paste boots, or possibly a light plaster encasement; (c) the local application of cold to the extremities; (d) the intravenous administration of hypertonic agents (plasma, glucose) to control transudation; and (e) the possible improvement of vasoconstrictor tone by the use of adrenaline.

Careful observations indicate that amputation revisions through the feet, as far back as the tarsometatarsal joints, have provided a satisfactory functional result for standing and adequate walking. In standing, the preservation of a stable tarsus sustains the mechanical arches of the feet, and ligaments and muscles act to balance the body weight on the tarsals. For walking, mobility at the metatarsophalangeal joints is necessary for the springlike take-off of each step. The spring-steel longitudinal strip in the sole of the shoe, and the transverse leather bar on the sole of the shoe, placed in back of the distal ends of the revised metatarsals, have materially improved walking. Insistence on continual care and hygiene of the feet should be stressed.

JOSEPH K. NARAT, M.D.

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

McCorkle, H. J., and Silvani, H.: Selection of the Time for Grafting of Skin to Extensive Defects Resulting from Deep Thermal Burns. *Ann. Surg.*, 1945, 121: 285.

Large areas that have been deeply burned should be covered with epithelium by means of skin grafts at the earliest opportunity. It is necessary, however, to wait until shock, alterations in body proteins,

fluid and electrolyte balance, renal function, edema, and "toxemia" have been controlled. Also, it is desirable to delay the grafting until the epithelium has been restored spontaneously to all areas of second-degree burns. To wait for epithelization of large full-thickness defects, however, even though they contain small viable epithelial islands that eventually might spread to cover the area, is usually unwise. Grafting should be done early enough to avoid the period of debilitation so often associated with the presence of large granulating areas several weeks after a severe burn. Maintenance of nutrition, with particular reference to a diet high in protein and vitamin C, is essential, especially if early skin grafting is contemplated.

It is difficult to designate an exact time that will satisfy all of these requirements. Surgical excision should be done in a fully equipped operating room, preferably at some time between the second and third weeks following the burn. The procedure of excision of burned tissues and early skin grafting may be used both for burned patients treated initially with a compression type of dressing, and those upon whom coagulum-producing drugs, such as tannic acid with silver nitrate or the dyes were used. A general anesthetic is required.

The burned area and surrounding skin are cleansed thoroughly with a detergent solution and draped with sterile linens. The proposed donor areas are prepared similarly, but separately. All necrotic tissue is excised, as much viable tissue being preserved as possible. This dissection is difficult and slow. It is preferable to apply skin grafts at the same operation if the condition of the patient permits, but occasionally it may be necessary to delay for a few days before placing the grafts at a second operation. Skin grafts of intermediate thickness are removed from donor sites, using the Padgett or Blair method, and are fixed to the denuded areas with cotton sutures. If the available donor sites do not provide enough grafts to cover the deficient areas completely, the grafts are cut into small squares (postage stamps), from 1.5 to 2 cm. in size, and are placed as near to one another as is possible over the entire defect, but they are not sutured. Donor grafted areas are covered with a single layer of fine-mesh gauze impregnated with a grease base containing a bland antiseptic ointment, and voluminous compression dressings are applied. In children, or in adults with burns near joints, a light plaster covering may be placed over the compression dressing. If possible, the original dressings are left in place for two weeks following the grafting procedure; if it becomes necessary to remove them earlier, the procedure should be carried out in the operating room, and a compression dressing should be reapplied at once.

Apparently, early grafting of skin following extensive deep burns minimizes contracture and deformity. Some patients will need no additional procedures, but others will require plastic correction of contractures that have resulted in spite of early grafting. For such patients the early closure of burn wounds by the application of grafts of intermediate thickness probably will permit earlier plastic repair.

JOHN E. KIRKPATRICK, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Walker, J. M., and Hamilton, J. W.: The Treatment of Actinomycosis with Penicillin. *Ann. Surg.*, 1945, 121: 373.

In 6 cases of actinomycosis favorable results were obtained with penicillin therapy although the follow-up periods are too short to claim permanent cure. Prolonged treatment, usually for from six to eight weeks, was required.

The authors believe that a combination of penicillin and sulfonamides might be employed to advantage, and stress the necessity of surgical excision in addition to penicillin when there is marked fibrosis and scarring. WALTER H. NADLER, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Levitin, J., and Weyrauch, H. B.: Acute Obstruction of the Colon. *Am. J. Roentg.*, 1945, 53: 132.

Acute colonic obstruction due either to cancer or volvulus presents definite distinguishable roentgenological findings which permit an accurate diagnosis.

In malignant lesions of the sigmoid the rate of tumor growth is slow and permits the bowel proximal to the tumor to maintain its tone and size while the back pressure dilates the cecum and the ascending colon.

On the other hand, volvulus of the sigmoid is a sudden twisting of the intestinal loop. This closed portion rapidly becomes distended with gas rising out of the bony pelvis and at times reaches to the diaphragmatic level.

Nine case reports with films and line drawings illustrating the views of the authors accompany the article. R. A. BERGER, M.D.

Kemp, F. H.: X-Rays in Diagnosis and Localization of Gas Gangrene. *Lancet*, Lond., 1945, 248: 332.

In the present war cases of gas gangrene have been far fewer than they were in the war of 1914 to 1918, but the disease still remains one of the principal causes of death from wounds.

War Memo No. 2 issued by the British Army in 1943 gives the early symptoms and signs of gas gangrene as follows:

1. Increasing pain in the wound area, with possibly the appearance or increase of local swelling.
2. A rising pulse rate in the absence of continued hemorrhage and after shock has been overcome.
3. A change in the mental attitude of the patient, which is difficult to define with accuracy; this change may be one of mental apathy or sometimes euphoria, with or without restlessness.
4. A wound which is relatively dry, or, at most, shows a thin discharge, the exposed muscle and fat at times being stained a plum color from hemolysis.

Occasionally, unexplained attacks of vomiting may occur in the early stages.

Unfortunately, not one of these signs alone is sufficiently distinctive, and if all are present together the patient's condition is already grave. Some method is required for examining suspicious cases which will establish an early diagnosis; with this some reduction in the fatality rate might be achieved.

The use of x-rays in the diagnosis of gas gangrene is not just a matter of detecting gas, for there are several causes other than gas gangrene which give rise to gas in the soft tissues.

All fresh wounds, even a tiny needle puncture, may permit air to enter the tissues. Sometimes gas crepitations may be detected clinically or bubbles may be seen in the depths of the wound, but in most cases air is not observed unless the part is roentgenographed. Air may extend throughout the entire length of a limb, but it never infiltrates the muscles unless it is forced in under pressure. The amount and distribution of air in the tissues vary according to whether the wound is open or closed, and with the amount of tissue which has been lost. If a wounded part is not immobilized, movements, active or passive, tend to suck air into the tissues.

In one of the author's recent cases a roentgenogram of the chest showed gas outlining the fibers of the pectoralis major muscle on the left side, as well as well marked subcutaneous emphysema in the neck and the left arm. The patient had a small penetrating wound of his chest in the pectoral region and with each breath he could be seen to blow air from his chest into the pectoral muscle. The roentgenographic picture of this muscle was very like the appearance given by fulminating gas gangrene.

Once the injured part is placed completely at rest, air is quickly absorbed. In twenty-four hours the amount is considerably less and within three days all but a trace has gone. The rate of absorption seems to vary in different tissues, being quicker from muscle and synovial membrane than from areolar tissues. If the tissue is dead there is no absorption.

Many other factors in treatment may influence the roentgenographic picture. Air can be introduced by changing a pack, removing a stitch, or by irrigation. In one case x-rays showed a great deal of air which had been introduced without the surgeon's knowledge during the manipulation of an intramuscular penicillin drip. Soft paraffin gauze tends to impair the absorption of air and holds it in pockets on the skin or in the wound. When the tissue spaces have become sealed off, manipulations do not usually suck more air into the tissues, but any subsequent operation may permit air to enter. Thus the treatment adopted must be considered when assessing the significance of gas bubbles in the tissues.

Local formation of gas in the depths of a wound by gas-forming organisms give a roentgenographic appearance which closely resembles that given by air. As a rule, it is impossible to differentiate this gas from air except by serial roentgenographic examinations, and only then if the observer is acquainted with all the details of the patient's treatment subsequent to his accident.

Local gas formation does not necessarily mean invasion of the living tissues by organisms, for, as a rule, the bubbles form in a hematoma, around a foreign body, or in dead tissue. In such cases there may be no clinical signs of infection, and the roentgenographic signs do not in themselves demand surgical intervention.

It is very difficult to decide when gas-forming organisms have begun to invade the loose cellular tis-

sues. The fact that the wound is dirty, inflamed, and foul smelling only means that an inflammatory reaction is taking place and does not necessarily show which organism is responsible. If gas can be felt crackling in the subcutaneous tissues, or can be seen bubbling from the depths of the wound, this does not mean that the gas is necessarily due to gas-forming organisms, for it may be air. Even the presence of anaerobic bacteria means nothing beyond the fact that the wound is infected, and many wounds so infected show no trace of gas. Anaerobic cellulitis almost always accompanies true gas gangrene, and gas formation in the loose cellular tissues is often detected roentgenographically in advance of an infection in the muscles, whereas clinically there is often but little indication of its presence except when the gas is subcutaneous.

Anyone who studies soft-tissue roentgenograms of the injured must be aware of the normal relative translucencies between the main groups of muscles; these are due to fat. In some cases, especially in old or middleaged people with flabby muscles, the roentgenograms show multiple linear streaks in the muscles which are due to fatty replacement; this picture at first sight may resemble the appearance of acute fulminating gas gangrene, but if care is taken to examine the whole limb, the observer will notice that the change is not confined to any one group of muscles and bears no relationship to the clinical signs. In a difficult case a roentgenogram of the opposite side will help by showing the same appearance. It is not widely known that after injury there are often local collections of free fat in the loose cellular spaces around the injured part. This fat is revealed as radiotranslucent patches or streaks in the tissues. As a rule the translucency is not so great as that produced by gas, but at times it is difficult to detect a difference.

When a surgeon discloses discolored and friable muscles in a wound which is two or three days old it may seem very suspicious to find bubbles of gas, but if there are no signs of invasion of the healthy tissue it is almost certainly safe to do no more than resect the damaged tissues. A doubtful case should be kept under constant clinical observation and repeated roentgenographic control.

In the heavier parts of the body it is easy to miss one or many gas bubbles in the tissues in a single anteroposterior projection. To avoid mistakes the greatest care must be taken to examine the patient clinically and rotate the limb or position the tube so that the suspected part is uppermost. A projection taken from the side is probably the most important.

The author made it a rule to re-examine every patient who complains of increasing local pain or discomfort in the tissues around his wound. As a rule, three-hourly examinations are sufficient, but in some instances, in which the clinical course changes rapidly, it may be necessary to examine the patient every hour. If a limb is encased in a plaster a roentgenographic examination is useless and the plaster should be removed.

There are no characteristic clinical signs of early gas gangrene. Crepitation is not a reliable guide. There is no reason why each case should not be examined roentgenographically. If the findings are suspicious the surgeon need do no more than keep the case under observation, but if the local condition does not improve, or grows worse, the examination should be repeated, for serial roentgenographic examinations offer incontestable evidence of gas formation.

JOSEPH K. NARAT, M.D.

Forssman, G.: Roentgen Diagnosis and Irradiation Treatment of Gastric Sarcomas, especially Lymphosarcomas and Reticulum-Cell Sarcomas (Ueber die Roentgendiagnostik und Strahlenbehandlung von Magensarkomen, insbesondere Lymphosarkomen und Retikulumzellensarkomen). *Acta radiol. Stockh.*, 1943, 24: 343.

The author reports on the good therapeutic results of x-ray treatment in 9 cases of gastric sarcoma at Radiumhemmet, Stockholm. Very instructive photographs of gross specimens and roentgenograms are added, and a comprehensive survey of the subject is given, including statistics, pathology, symptomatology, therapy, and the bibliography up to 1940.

From 1 to 2 per cent of the malignant gastric tumors are sarcomas. They occur at all ages and are more frequent in men than in women. The site of preference is the greater curvature, in contradistinction to the carcinomas. Histologically, the majority of these tumors are either lymphosarcomas or reticulum-cell sarcomas, and they probably originate from the lymph follicles of the submucosa, other forms being rarer. The tumors spread in the submucosa, and the circumstance that the mucosa remains intact for a long time causes its typical bulging outline with its uniformity and the early disturbances in peristalsis due to infiltration of the muscularis. The frequently smooth surface of the sarcoma, its soft and flexible edges, the central crater, and the multiplicity sometimes found, as well as the radiosensitivity of the tumor, indicate the diagnosis of sarcoma. Metastases occur early, more frequently by way of the lymph than of the blood circulation, and may be found in the regional lymph nodes as well as in almost any organ. According to most authors, the prognosis is poor, only from 10 to 15 per cent of the cases surviving for more than five years. The clinical symptoms are less typical than in stomach carcinoma; symptoms of obstruction, hematemesis, and melena occur rarely.

The reticulum-cell sarcomas do not grow into the omentum or the peritoneal cavity; therefore they are rarely palpable before operation. Although some degree of anemia and loss of weight accompany the tumor, cachexia develops very late. A palpable tumor in a younger person in good general condition is, therefore, suggestive of sarcoma.

To secure an early diagnosis, the roentgenological findings are most helpful. The typical signs are: localization different from carcinoma, partly in the lumen, and partly within the wall of the stomach;

spread in the submucosa without lesion of the mucosa, and early disturbances of the peristalsis.

As to the therapy, the author suggests early surgery, preferably radical resection, even in those cases in which regional lymph-node metastases are found, as these can be taken care of by postoperative irradiation.

All of the 9 cases were treated postoperatively with x-rays. The results were very encouraging indeed as compared with the high mortality rate reported by other authors. Six cases were cured permanently, only 3 very advanced and inoperable cases terminated fatally. Most impressive is the report on an inoperable reticulum-cell sarcoma in a man of thirty-three years. A total dose of 5,250 roentgens was given in two series (series 1—4,250 roentgens during fifty-seven days, and series 2—1,000 roentgens during thirteen days). The patient recovered and was free of symptoms and able to work two and one-half years after the operation. Palpation in connection with a later appendectomy also revealed the stomach to be free from any tumor. Operable cases were treated with gastric resection and postoperative roentgen therapy with daily doses of 250, 300, or 400 roentgens with a ½ copper or tin filter, from 50 to 60 cm. focal distance, and a total cutaneous dose of from 2,500 to 3,000 roentgens during from four to six weeks on each of two anterior and two posterior fields. Supplementary series were given in two or three months later in some cases.

Preoperative roentgen treatment is desirable and would probably further improve the results, but in most cases it is hindered by the difficulty of the diagnosis.

Many cases of sarcoma are still often wrongly diagnosed as inoperable cancer on the basis of exploratory laparotomy, and thus are not benefited by the radiotherapeutic possibilities. Therefore, biopsy should always be done in cases of inoperable tumors. WERNER M. SOLMITZ, M.D.

Mustakallio, S.: Carcinoma of the Larynx and Hypopharynx; Roentgen Treatment and the Results of Therapy (Ueber das Larynx- und Hypopharynxkarzinom, ihre Roentgenbehandlung und die Ergebnisse der Therapie). *Acta radiol. Stockh.*, 1944, 25: 13.

The material reported by the author comprises 238 cases of carcinoma of the larynx and hypopharynx treated at the central Institute for Radiotherapy in Helsinki, Finland, since the foundation of the Institute in 1936.

The author does not divide his patients according to the location of the point of origin of the new growth in the manner that is commonly used by laryngeal surgeons, and this for two reasons: (1) because the condition in most of his patients was already so far advanced when they came under his care that it was often difficult or impossible to determine the exact point of origin, and (2) because the type of laryngeal tissue, *i. e.*, the matrix of the cancer, is not so important in irradiation treatment. He does, however, divide his carcinomas into the laryngeal and the hypopharyngeal, the dividing line between the larynx and hypopharynx being taken as the free edge of the epiglottis, down along the aryepiglottic folds to the arytenoid cartilages in the back.

The difficulties of classifying these advanced forms of cancer caused the author to create temporarily a third class or group of these tumors, consisting of tumors involving the epiglottis and adjacent areas, exclusive of cancers of the base of the tongue. These cancers he designated as cancers of the anterior wall of the larynx. This group exhibited two notable characteristics: (1) 70 per cent of them disclosed metastasis to the region of the neck when they came under treatment, and (2) they were found only in male patients, as against 3 females in the group of 130 laryngeal carcinomas; of the hypopharyngeal tumors, 15 occurred in women. The absence of females with this type of tumor and the paucity with the two other types of throat cancer is tentatively explained by the author on the etiological basis of this type of cancer in general, that is, Finnish women do not smoke very much, and the Plummer-Vinson syndrome is extremely rare in the women of Finland. Another justification for creating this class of cancers of the anterior wall of the larynx, although many of them probably originate in the hypopharynx, lies in the fact that they more closely resemble the true laryngeal tumor in their response to irradiation treatment; for example, of the 130 patients with laryngeal carcinoma, 38 lived five or more years, and of these, 9 were free of symptoms (a cure rate of 24 per cent), while of 71 patients with tumor of the anterior laryngeal wall, 28 lived for five years or more, and of these 12 were free of symptoms (a rate of absolute cure of 43 per cent).

For the purpose of evaluating the results of treatment, therefore, all cases of tumor of the larynx, including tumor of the anterior wall, were thrown together as cases of tumor of the larynx to make a total of 238. Seventy-eight of the patients were living after five years or more, and 22 of these were cured, a rate of 28 per cent, while of 37 patients with lypopharyngeal cancer, 12 were still living after five years or more, but only 1 of these could be classed as cured, an absolute cure rate of only 8 per cent. Even so, however, if all these cases are considered together, we would still have 22 absolute cures among 78 five-year survivals, an absolute cure rate of 28 per cent. These results compare favorably with the best results of surgery, when one refers to Weber's collected figures showing that 287 (27 per cent) of 1,174 patients were free of symptoms after three years following various operations for cancer of the laryngeal region.

In the attainment of the above results, naturally, large dosages were employed in the treatment, which was almost exclusively roentgentherapy: Siemens' Stabilivolt apparatus; 180 kv., 4 ma.; focal distance 40 cm.; filter of tin (Thoraeus); size of field, 6 by 8 cm. or, more rarely, 8 by 10 cm. Most frequently

two lateral fields were used, with a small anterior field added occasionally; when there were large metastases in the region of the neck a posterior field on the side of the metastasis was adjoined. Daily dosages consisted in general of 250 roentgens, but as much as 300 roentgens have been employed. All roentgen dosages were calculated against the skin. The total dosages varied from 6,000 to 7,000 roentgens, and the total period of treatment thus lasted about a month.

With such dosages, of course, severe reactions in the tissues of the throat must be expected, and the author believes that some patients have eventually died of pulmonary complications resulting from the atrophies and cicatricial changes due to the irradiation itself. Nevertheless, he believes that the results obtained in cases of carcinoma of the larynx are so favorable that roentgentherapy should be the treatment of choice with this type of cancer and that surgical intervention should be performed only as an additional measure. JOHN W. BRENNAN, M.D.

Eker, R., and Poppe, E.: Primary Bone Sarcoma. *Acta radiol.*, Stockh., 1942, 23: 387.

From May, 1932 to September, 1937 a total of 3,795 patients with malignant tumors were treated at the Norwegian Radium Hospital. Of these, 42, or 1.1 per cent, represented cases of primary sarcoma of bone.

In the present article the authors analyze the various aspects of bone sarcoma and compile statistically 41 of the 42 cases observed. One case was not followed up. In 32 cases there was microscopic confirmation; in the others the roentgen appearance and subsequent clinical course constituted the criteria of diagnosis.

The following classification was used in this series of tumors:

1. Osteogenic series: (a) osteoblastic (including sclerosing), 18 cases; (b) osteolytic, 4 cases.
2. Chondroma series: (a) chondrosarcoma, 7 cases; (b) myxochondro-osteosarcoma, 3 cases.
3. Ewing's sarcoma, 5 cases.
4. Periosteal fibrosarcoma, 4 cases.
5. Unclassified, 1 case.

The irradiation consisted of protracted fractionated roentgen therapy except in 1 of the cases in which radium was used. The technical factors were: 175 kv., 2 mm. of copper, 1 mm. of aluminum, 4 ma., 60 cm. skin target distance, 5 roentgen minutes, 200 to 450 roentgens in air per seance, 3 or more fields for cross-firing, 4,000 to 4,500 roentgens per field, or, if only from 1 to 2 fields were used the total dose per field was slightly higher. In some cases a second series of irradiation was undertaken from three to four months later with a total dose of from 2,000 to 3,000 roentgens per field.

The authors recommend that a combination of surgery and radiation therapy be used, whenever possible, in all groups of bone sarcoma, with the exception of Ewing's sarcoma in which irradiation alone is advisable.

In the osteogenic series, 3 out of 22 patients lived five years or longer after the first treatment; in the chondroma series, 2 out of 10; in the Ewing's sarcoma series, 1 out of 5; and in the periosteal fibrosarcoma series of 4, none lived as long as five years. Thus, for the entire series the five-year survivals amounted to 6, or nearly 15 per cent.

The authors give several tables in which they have compiled in detail the method of treatment, the age and sex distribution, as well as the site of the primary tumor in the various groups. Five of the 6 cases with survival for five years or longer are described in brief résumés, and the respective roentgenograms and photomicrograms are included for the purpose of illustration. T. LEUCUTIA, M.D.

MISCELLANEOUS

Chydenius, J. J.: Radiation Injuries of the Intestine and Urinary Bladder Caused by Radium Treatment of Carcinoma of the Uterine Cervix (Strahlenschaeden des Darmes und der Harnblase bei der Radiumbehandlung des Carcinoma colli uteri). *Acta radiol. Stockh.*, 1942, 23: 1.

The author discusses a series of 321 cases of cervical carcinoma treated by irradiation with radium. In 33 of these cases, there were severe reactions of the urinary bladder, rectum, or contiguous structures (ulcers, strictures of the rectum, rectovaginal or vesicovaginal fistulas). The interval between the radium therapy and the onset of the complications varied from five to thirty months. The distance between the tumor and the rectum varied considerably, and therefore the doses delivered in the rectum were subject to great variations. The method of measuring with the dosage in terms of milligram hours is unsatisfactory as it does not with certainty avoid injury to the contiguous structures. The variations in the position of the rectum were demonstrated in roentgenograms.

There is much room for improvement of the dosage calculation of focal doses in radium, as well as in roentgen therapy. In this connection, the author draws attention to the article he published in 1940 in the *Acta Obstetrica et Gynecologica Scandinavica*, 20: fasc. 2, dealing with the radiohistological examinations, and the isodore curves, calculated in roentgen units, which were published in that article and may be used for the afore-mentioned purposes.
WERNER M. SOLMITZ, M.D.

Cooper, A. G. S., and Robertson, D. F.: The Treatment of Postirradiational Ulcers by Radon Ointment. *Med. J. Australia*, 1945, 1: 297.

The treatment of postirradiational ulcers which are constantly being observed in radiotherapeutic clinics, constituted in the past a difficult and disturbing problem. The adoption by the authors in 1943 of the application of radon-impregnated vaseline as outlined by Uhlmann has solved the problem at the Brisbane General Hospital in all cases except those due to overdosage.

To understand the rationale of the treatment it is necessary to explode 3 misconceptions: (1) that radon ointment adds further damage to an area already too heavily irradiated (The necrosis is not a direct sequel to irradiation but a result of the inadequate blood supply of scar tissue, similar to that observed in keloids following burns or in simple surgical scars. Small doses of radon, in a concentration less than one-twentieth of that required to produce erythema in the same time, allow complete recovery of the cells in all these instances); (2) that tissue recovery is due to the alpha rays of the ointment (The ionization density of the beta and gamma rays which are also emitted during the process of decay of the radon is less than one one-hundredth of that from the alpha rays); and (3) that the ointment, in the strength used, has no effect on a malignant lesion.

It is the authors' impression that the alpha rays in small doses stimulate and promote the growth of vascular epithelial tissues. There may be a parallel in the effect of very small doses of roentgen rays in the treatment of inflammatory lesions.

The authors prepare their ointment by breaking ordinary radon seeds (1 cm. long and with a 0.5 mm. gold wall) in a jar of hot "vaseline" (melting at 44°C). Mixing is performed by melting and shaking after the jar has stood for twenty-four hours. The contents are tested for uniformity of distribution by fluorescence in the dark, and the activity is checked by measurement of the gamma rays emitted by the full jar before use.

This freshly prepared ointment is then applied liberally with a spatula to the ulcer to be treated and about 1 cm. of normal skin surrounding it. The thickness of the ointment is immaterial since the alpha particles have a range of only a fraction of a millimeter in vaseline, but a layer of from 2 to 3 mm. will guard against the loss of radon and thus insure a more uniform strength during the entire application. The ointment is covered by a rubber dam or cellophane, the edges of which are secured to the skin by adhesive plaster to prevent diffusion of the radon gas.

The concentration of the ointment varies from 0.024 to 0.060 mc. per gram of "vaseline." As a rule, applications are left on for eight hours and repeated once a week for three on an average. The addition of 10 per cent lanolin to the ointment makes no difference as far as the penetration of the radon into the tissues is concerned. In the interval between the radon treatments unguentum acidi borici (10 per cent) or unguentum olei morrhuae with vaseline are applied.

Altogether 69 ulcers were treated. Of these, 20 proved to be recurrences of the original malignant lesion; 41 have been completely healed and 8 improved to such an extent as to be no longer suspected of being recurrences. No example of simple necrosis has failed to respond. In fact, a lack of response constitutes an almost sure sign of malignant recurrence.

The authors also used the method in 7 recalcitrant cases of chronic varicose ulcer totaling 15 separate areas. Nine areas healed promptly, 5 improved, and only 1 failed to show any response. Three chronic ulcers in scars following burns and surgery, in which no radiation therapy had been given, likewise healed completely.

Two case reports are included in brief résumés to illustrate the method of procedure and the subsequent clinical course of healing.

The conclusion is drawn that the excellent immediate results well justify the use of the radon ointment, not only in postirradiational ulcers but also in other benign chronic ulcerative lesions. The time is too short as yet to assess the permanency of the results. It is believed, however, that the field of application could be extended and that the method may also be of assistance in military surgery.

T. Leucutia, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Saltonstall, H., Walker, J., Jr., Rhoads, J. E., and Lee, W. E.: The Influence of Local Treatment of Burns on Liver Function. *Ann. Surg.*, 1945, 121: 291.

The relation of the local treatment of burns to hepatic damage, which in the past has been approached either by animal experiments or by a study of the pathological changes found in fatal cases at autopsy, suggested to the authors a study concerned primarily with the functional changes in the liver. Most of the patients survived. It is important to determine the effect on liver function of not only tannic acid, but also other tanning agents. Two other questions are of considerable interest: (1) is the hepatic damage following the use of tannic acid locally a cause of increased mortality, and (2) is the hepatic damage following burns entirely due to therapeutic agents used in the local treatment of the burned areas?

The selection of liver-function tests is difficult since the liver plays an important role in so many metabolic processes. In addition, the liver has a large reserve and rapid powers of regeneration, so that much liver damage may occur before any change can be demonstrated by liver function tests. The authors used the Van den Bergh test, the bromsulfalein retention and the hippuric-acid-excretion tests, and flocculation of a cephalin-cholesterol emulsion in this series of patients.

Tannic acid was so well established in burn therapy that it, or one of the other tanning methods, had largely displaced other methods of local therapy in this country and, to a considerable extent, abroad. Emphasis on its hepatotoxic properties, by Wells and his coworkers, came at a time when the visceral changes following burns were becoming of increasing importance, probably as the result of improvements in the treatment of shock. However, taken in conjunction with the autopsy data reported by Erb, Farmer, and Morgan, there can be little doubt that the tannic acid used in burn therapy is absorbed sufficiently to increase the hepatic damage.

The mildness of the changes in hepatic function seen in most of the cases treated locally by Koch's method is very gratifying; and while the changes are still definite, it would seem that the predominance of hepatic damage in burn toxemia, as described by Wilson, McGregor and Stewart, and Pack, has been due largely to tanning agents.

The question of whether tannic acid actually caused the deaths of burned patients cannot be answered completely. In this series no patients with burns of less than 40 per cent died after tannic-acid therapy except one who was proved at autopsy to have had an advanced septicemia.

A significant aspect of the authors' experience, however, has been the fact that since tannic acid was discarded, no patients have survived burns of over 40 per cent of the body surface, and only 2 have survived burns of 35 per cent or over. It seems likely, therefore, that while tannic acid may increase liver damage when used in the local treatment of extensive burns, its use has not been attended by greater mortality.

JOHN E. KIRKPATRICK, M.D.

GENERAL BACTERIAL, PROTOZOAN, AND PARASITIC INFECTIONS

Fisher, A. M.: The Therapeutic Value of Penicillin Applied Locally, Based on Experience with the Crude Material in a Variety of Infections. *Bull. Johns Hopkins Hosp.*, 1945, 76: 134.

Any ideal antibacterial agent for local application should show: (1) high solubility in normal and pathological body fluids; (2) no inhibition by these body fluids; (3) no toxicity to the cells locally nor to the body generally; (4) no production of local and general hypersensitivity; (5) rapid action against all bacteria in high dilutions, and (6) stability of solution.

Such a perfect antibacterial substance fulfilling all these criteria has not been found as yet. Sulfonamides are only bacteriostatic and are inhibited by pus; they probably also produce generalized hypersensitivity. Tyrothricin is limited by its selective action against gram-positive cocci and by high systemic toxicity. Penicillin is highly soluble in water, saline solution, and body fluids; it is not inhibited by any body fluids nor by p-aminobenzoic acid; it is not toxic, local reactions being extremely rare, and general hypersensitivity reactions have rarely been reported. The chief drawbacks of penicillin are relative instability and limitation to certain bacteria, such as the staphylococci (except 10 per cent resistant strains), streptococci (nearly all), anaerobic streptococci, meningococci, pneumococci, gonococci, clostridia welchii, and corynebacteria diphtheriae. The resistant bacteria are the escherichia coli, eberthella typhosaus, bacillus proteus, pseudomonas aeruginosa (pyocyaneus), bacillus alkaligenes, alpha streptococcus fecalis, haemophilus influenzae, aerobacter aerogenes, and Friedlander's bacillus. Some of these resistant bacteria produce a "penicillinase" which is capable of neutralizing penicillin.

A number of investigators have reported favorable clinical trials with the local use of penicillin, in different forms and concentrations, for infections of the eye, mastoid, wounds and sinuses, and in burns, war wounds, brain wounds, empyema, and osteomyelitis.

The author used first the "Fleming" strain of penicillin and later the "RC-2" strain, as unrefined culture filtrate. The latter proved to be about

doubly potent with an average of 100 units per cubic centimeter. Generally the procedure was as follows: (1) culture of the wound; (2) wide incision of the wound, with removal of dead tissue when necessary; and (3) continued saturation of the wound with penicillin until the surrounding tissues start the process of repair.

Ninety-five cases treated with crude penicillin are reported; some patients received injections of penicillin along with local applications of the drug. The diagnoses were osteomyelitis of the long bones, chronic and acute frontal-bone osteomyelitis, streptococcal throat infections (including streptococcus carriers), wound infections, and eye infections.

The total results were good in 63 per cent, poor in 13 per cent, and indefinite in 24 per cent. Concentrations of from 25 to 100 units per cubic centimeter were used and were considered sufficient, since dilutions of 0.16 units per cubic centimeter have been shown to kill staphylococci, streptococci, and pneumococci in vitro.

Careful bacteriological determination of penicillin sensitivity of the infecting bacteria should always precede actual treatment; when infection is deeper, the combination with the systemic use of penicillin or with sulfonamides or tyrothricin may be advisable. These drugs are compatible in combinations.

The local application of penicillin for a localized infection appears more economical and efficient, provided the lesion is open and the infection not too deep; but general surgical principles, such as drainage of pus, removal of sequestra, and excision of dead tissue, must not be neglected.

ARTHUR J. LESSER, M.D.

DUCTLESS GLANDS

Guerkan, K. I.: Chronic Thyroiditis and Primary Thyrotoxicosis (Exophthalmic Goiter). *Arch. Surg.*, 1945, 50: 125.

The author reports the case of a fifty-six-year-old male who had a stony-hard thyroid that was diagnosed preoperatively as carcinoma. The basal metabolic rate was +87 and there was exophthalmos along with the classical symptoms of thyrotoxicosis. A subtotal thyroidectomy was performed. The histological diagnosis was chronic thyroiditis.

The author presents this case because of the extreme rarity of exophthalmic goiter associated with chronic thyroiditis. EARL O. LATIMER, M.D.

Bartels, E. C.: The Use of Thiouracil in the Preoperative Preparation of Patients with Severe Hyperthyroidism. *Ann. Int. M.*, 1945, 22: 365.

The author reports results in 64 cases of hyperthyroidism treated with thiouracil and subsequently operated upon at the Lahey Clinic. The patients were severely toxic and would have been poor operative risks if prepared with Lugol's solution alone.

Early experience led to the conclusion that under thiouracil, patients should not be sent for operation until a normal or nearly normal basal metabolism is recorded. The time required to reduce the basal metabolism is roughly one day for each per cent to be reduced. In this series, the average pretreatment basal metabolism rate was +51 per cent, and an average of fifty-eight days was required for lowering the metabolism to the proper level for surgery. Those patients who had previously received Lugol's solution required a longer treatment with thiouracil. There was an average gain in weight of 13 pounds; the greatest gain was 30 pounds. The treatment of patients without heart failure was ambulatory, with examination and a blood count every two or three weeks. Patients with heart failure were hospitalized.

With thiouracil treatment alone, the thyroid gland at operation was found to be soft and friable and to bleed excessively, which increased the operative difficulty considerably. This was overcome by starting iodine administration as soon as the basal metabolism rate had reached +20 per cent, continuing thiouracil for another three weeks, and then giving iodine alone for one week before surgery. The anesthesia and postoperative course were uneventful.

Toxic reactions were encountered in 8 of 119 cases. Only 1 of these was included in the 64 cases of the present report. One patient exhibited a skin eruption, 4 had fever, and 3 developed leucopenia. In every instance, symptoms of thiouracil intoxication subsided on discontinuance of the drug.

The average hospital stay under thiouracil was from seven to ten days; under Lugol's solution alone, several weeks. CLINTON H. THIENES, M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Webster, A., Stenhouse, E., Parsons, E., Phillips, A., and Others: A Step in Cancer Control. *Illinois M. J.*, 1945, 87: 119.

The sharp increase in deaths from cancer is readily understandable because of the increase in skill in modern diagnosis and the prolonged life span. In order to improve the statistics for treatment, diagnosis must be made early and adequate treatment begun while there is a chance to destroy the neoplasm.

The cancer-control clinic setup in Chicago is sponsored by the Illinois Division of the Field Army for the control of cancer, and the purpose of the clinic is to provide periodic examinations for apparently well women in an attempt to detect early cancer or precancerous lesions. No treatments are given in the clinic. If suspicious lesions are noted, the patient is referred to her family physician for further diagnostic investigation and for care.

Each patient is seen in the clinic twice. On the first visit a detailed medical and social history is taken and a complete physical examination is made. The laboratory work includes urinalysis, complete blood counts and serology tests, cervical and urethral smears, and chest fluoroscopy. On the second visit the results of the initial examination are interpreted for the patient and she is advised to consult her own physician if any other investigation is indicated.

TABLE I.—PELVIC FINDINGS

Condition	Number of Cases
External Genitalia	
Kraurosis	1
Senile pruritis and vaginitis	16
Sebaceous cyst of labia	3
Lichenification	1
Enlarged bartholin gland	4
Urethral caruncle	3
Vaginal cyst	1
Cystocele (with symptoms)	29
Cervix	
Lacerated or hypertrophied	16
Erosions	73
Polyps	19
Trichomonas	5
Corpus	
Retroverted	18
Fibroids	35
Prolapse	13
Adnexal mass or enlarged ovary	
Right side	4
Left side	5
Bilateral	5
Tumor of abdominal wall	1
Stricture of the vagina	1

The purpose of this article is to report the results of the examination of the first 600 patients.

Skin. Two hundred and one of the total patients were seen by the dermatologist, and of this group 8 had clinically diagnosable skin carcinomas, 5 had suspected melanomas, and 12 had precancerous dermatoses. Eighty-five patients had pigmented and nonpigmented nevi, and many other patients had minor skin conditions.

Breast. There were 10 proved cases of carcinoma of the breast among the 600 patients. The breasts were examined by palpation and transillumination, and when biopsy was considered to be indicated the patients were referred to their own physicians. Forty-two women complained of sensitive breasts or pain in the breast and in 75 per cent of these no abnormalities were noted. In only 3 of the 42 cases was there a palpable mass. Twenty-six patients complained of lumps in the breast; 8 of these had cystic mastitis and 4 had carcinoma. In 5 instances, tumors of the breast of which the patient was not aware were found; 4 of these were malignant. Of 19 patients in whom biopsy was requested, 18 were subjected to the procedure.

Pelvis. Only 16.4 per cent of the 600 women complained of pelvic symptoms. Bimanual examination and visualization of the vagina and cervix with a strong light was carried out by a trained gynecologist. The pelvic findings are listed in the accompanying table.

None of the cervical polyps proved to be malignant when biopsied. Among 73 cervical erosions there was no report of malignancy in the 7 cases in which a biopsy was advised. Twelve patients who complained of vaginal bleeding not associated with menstrual periods were examined. In 6 upon whom dilatation and curettage were done and reports were received, no malignancy was found.

One patient had an inoperable pelvic malignancy and another had an early adenocarcinoma of the body of the uterus. These were the only malignant conditions found.

Fluoroscopic findings. On routine chest fluoroscopy 402 of the patients had no unusual findings. Of the remaining women, 117 had abnormal cardiac shadows, 37 abnormal lung markings, and 16 abnormal skeletal changes. No tuberculosis was found.

Gastrointestinal tract. One patient had a cauliflowerlike carcinoma in the rectal ampulla; 5 had benign tumors; 22 had hemorrhoids, and the remainder of the entire group of 152 had minor rectal conditions.

Eye. Fourteen of the 600 patients were found to have one or more pigmented nodules on the iris of each eye, and 10 in only one eye. No ocular tumors were found. J. ROBERT WILLSON, M.D.